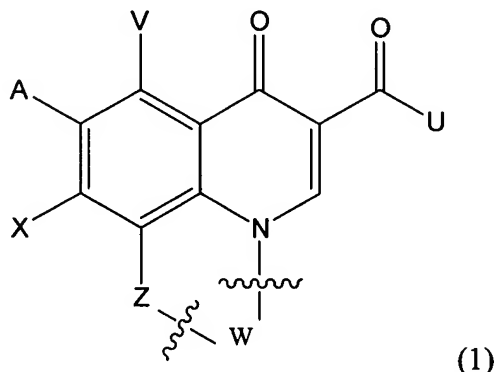


AMENDMENTS TO THE CLAIMS

1. (currently amended): A compound having formula 1, or pharmaceutically acceptable salts thereof



and pharmaceutically acceptable salts, esters and prodrugs thereof;

wherein V is H, halo, or  $\text{NR}^1\text{R}^2$  or  $\text{NR}^1 - (\text{CR}^1_2)_n - \text{NR}^3\text{R}^4$ ;

A is H, fluoro, or  $\text{NR}^1_2$ ;

Z is O, S,  $\text{NR}^1$  or  $\text{CH}_2$ ;

U is  $\text{OR}^2$  or  $\text{NR}^1\text{R}^2$  is selected from the group consisting of  $\text{NR}^1 - (\text{CR}^1_2)_n - \text{NR}^3\text{R}^4$  or  $\text{NR}^1\text{R}$  wherein  $\text{R}^1$  and R in  $\text{NR}^1\text{R}$  may form an optionally substituted 5-14 membered ring containing N, O or S;

X is  $\text{OR}^2$ ,  $\text{NR}^1\text{R}^2$ , halo, azido, or  $\text{SR}^2$ ;

n is 1-6 +3;

wherein  $\text{R}^1$  and  $\text{R}^2$  together with N in  $\text{NR}^1\text{R}^2$  and  $\text{R}^3$  and  $\text{R}^4$  together with N in  $\text{NR}^3\text{R}^4$  may independently form an optionally substituted 5-6 membered ring containing N, and optionally O or S a double bond or a ring, each of which is optionally substituted;

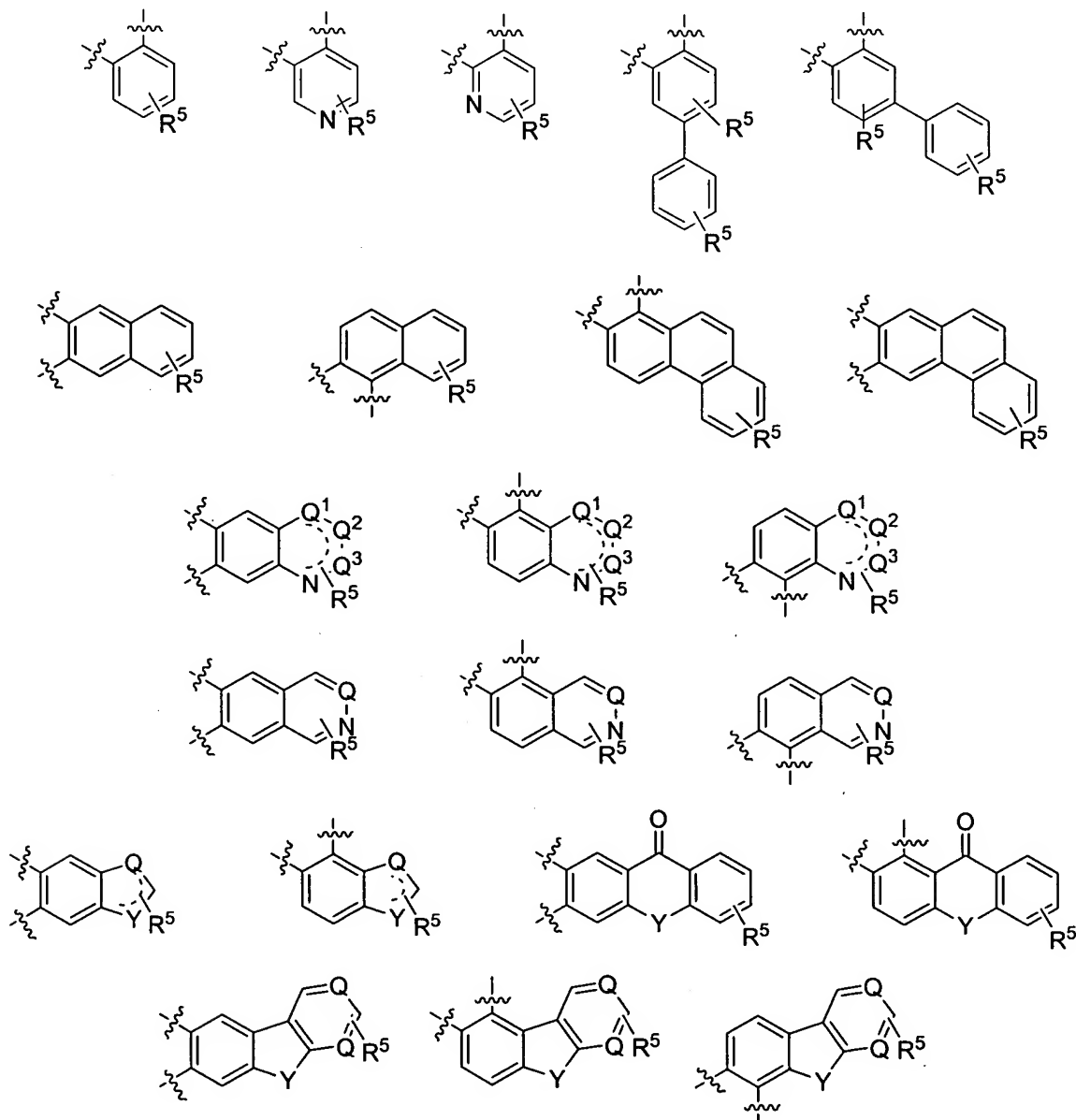
R is an optionally substituted 5-14 membered heterocyclic ring containing one or more N, O or S; or a  $\text{C}_{1-10}$  alkyl or  $\text{C}_{2-10}$  alkenyl optionally containing one or more non-adjacent heteroatoms selected from N, O, and S, and optionally substituted with a carbocyclic or heterocyclic ring;

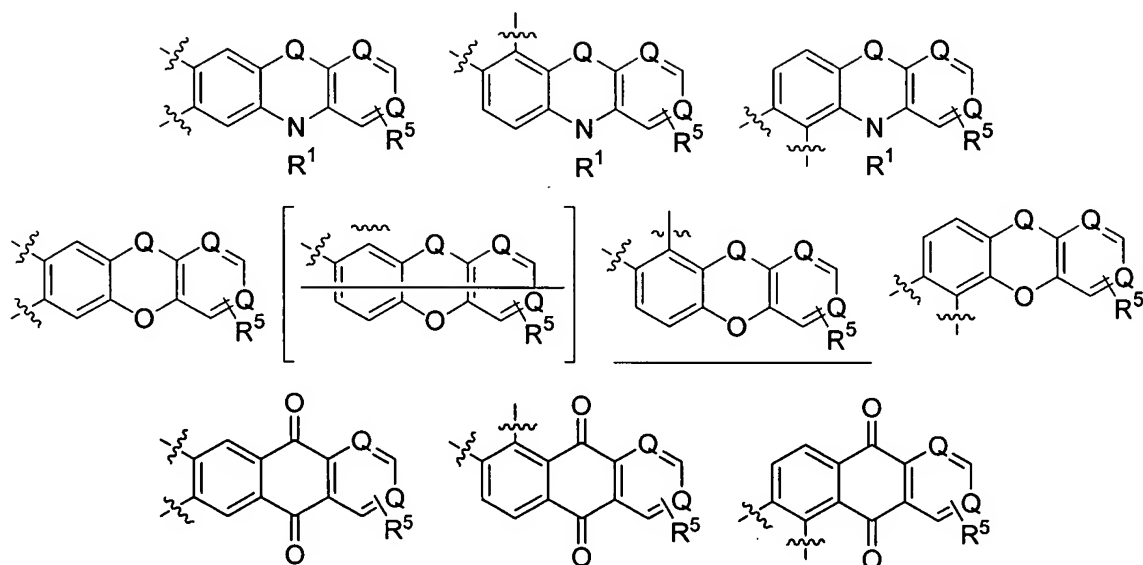
$\text{R}^1$  and  $\text{R}^3$  are independently is H or a  $\text{C}_{1-6}$  alkyl;

$R^2$  and  $R^4$  are independently is H or a  $C_{1-10}$  alkyl or  $C_{2-10}$  alkenyl optionally containing one or more non-adjacent heteroatoms selected from N, O, and S, and optionally substituted with a carbocyclic or heterocyclic ring; or

$R^2$  is an optionally substituted heterocyclic ring, aryl or heteroaryl;

W is selected from the group consisting of





wherein Q, Q<sup>1</sup>, Q<sup>2</sup>, and Q<sup>3</sup> are independently CH or N;

Y is independently O, CH,  $[[=O]]$  C=O or NR<sup>1</sup>;

and R<sup>5</sup> is a substituent at any position on the fused ring; and is H, OR<sup>2</sup>, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, each optionally substituted by halo, or C=O or one or more heteroatoms; ~~or R<sup>5</sup> is an inorganic substituent~~; or two adjacent R<sup>5</sup> is linked to obtain a 5-6 membered substituted or unsubstituted carbocyclic or heterocyclic ring, optionally fused to an additional substituted or unsubstituted carbocyclic or heterocyclic ring;

~~provided that U is not OR<sup>1</sup> when X is pyrrolidinyl; A is F; Z is O; and W is naphthalenyl or phenylene;~~

~~U is not morpholinyl or 2,4-difluoroaniline when X is F or pyrrolidinyl; A is F; Z is O; and W is phenylene; and~~

~~further provided that if U is OH, then W represents multiple fused aromatic rings and X is not halo; and X is NH<sub>2</sub>, or a moiety that does not contain N, or contains more than 6 carbons~~

wherein each optionally substituted moiety is substituted with one or more halo, OR<sup>2</sup>, NR<sup>1</sup>R<sup>2</sup>, carbamate, C<sub>1-10</sub> alkyl, C<sub>2-10</sub> alkenyl, each optionally substituted by halo, C=O, aryl or one or more heteroatoms selected from N, O and S; or is substituted with an aryl, a carbocyclic or a heterocyclic ring.

2. (original): The compound of claim 1, wherein A and X are independently halo.

3. (original): The compound of claim 2, wherein said halo is fluoro.
4. (original): The compound of claim 1, where V is H.
5. (currently amended): The compound of claim 1, wherein ~~U and X are independently~~ is NR<sup>1</sup>R<sup>2</sup>.
6. (currently amended): The compound of claim 5, wherein R<sup>1</sup> is H and R<sup>2</sup> is a C<sub>1-10</sub> alkyl optionally containing N, O or S ~~one or more heteroatoms~~, and optionally substituted with a C<sub>3-6</sub> cycloalkyl, aryl or a 5-14 membered heterocyclic ring containing one or more N, O or S.
7. (original): The compound of claim 6, wherein said 5-14 membered heterocyclic ring is selected from the group consisting of tetrahydrofuran, 1,3-dioxolane, 2,3-dihydrofuran, tetrahydropyran, benzofuran, isobenzofuran, 1,3-dihydro-isobenzofuran, isoxazole, 4,5-dihydroisoxazole, piperidine, pyrrolidine, pyrrolidin-2-one, pyrrole, pyridine, pyrimidine, octahydro-pyrrolo[3,4-*b*]pyridine, piperazine, pyrazine, morpholine, thiomorpholine, imidazole, imidazolidine-2,4-dione, benzimidazole, 1,3-dihydrobenzimidazol-2-one, indole, thiazole, benzothiazole, thiadiazole, thiophene, tetrahydro-thiophene 1,1-dioxide, diazepine, triazole, guanidine, diazabicyclo[2.2.1]heptane, 2,5-diazabicyclo[2.2.1]heptane, and 2,3,4,4a,9,9a-hexahydro-1H- $\beta$ -carboline.
8. (original): The compound of claim 5, wherein R<sup>1</sup> is H and R<sup>2</sup> is an aryl or a 5-14 membered heterocyclic ring containing one or more N, O or S, each optionally substituted with an amino or another heterocyclic ring.
9. (original): The compound of claim 8, wherein said 5-14 membered heterocyclic ring is selected from the group consisting of tetrahydrofuran, 1,3-dioxolane, 2,3-dihydrofuran, tetrahydropyran, benzofuran, isobenzofuran, 1,3-dihydro-isobenzofuran, isoxazole, 4,5-dihydroisoxazole, piperidine, pyrrolidine, pyrrolidin-2-one, pyrrole, pyridine, pyrimidine, octahydro-pyrrolo[3,4-*b*]pyridine, piperazine, pyrazine, morpholine, thiomorpholine, imidazole,

imidazolidine-2,4-dione, benzimidazole, 1,3-dihydrobenzimidazol-2-one, indole, thiazole, benzothiazole, thiadiazole, thiophene, tetrahydro-thiophene 1,1-dioxide, diazepine, triazole, guanidine, diazabicyclo[2.2.1]heptane, 2,5-diazabicyclo[2.2.1]heptane, and 2,3,4,4a,9,9a-hexahydro-1H- $\beta$ -carboline.

10. (currently amended): The compound of claim 5, wherein  $R^1$  and  $R^2$  together with N in  $NR^1R^2$  form an optionally substituted ~~[[5-14]]~~ 5-6 membered ring containing one or more N, O or S.

11. (currently amended): The compound of claim 10, where  $NR^1R^2$  is pyrrolidine, imidazole, pyridine, morpholine, thiomorpholine, piperazine, piperidine or diazepine.

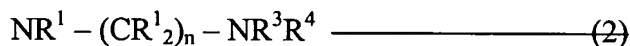
12. (canceled)

13. (currently amended): The compound of claim 1 ~~12~~, wherein n is 2-3.

14. (currently amended): The compound of claim 1 ~~12~~, wherein  $NR^3R^4$  is an acyclic amine, or guanidinyll or a tautomer thereof; ~~or  $R^3$  and  $R^4$  optionally form a substituted ring containing one or more N, O or S.~~

15. (currently amended): The compound of claim 1 ~~12~~, wherein  $NR^3R^4$  is morpholine, thiomorpholine, imidazole, pyrrolidine, piperazine, pyridine or piperidine.

16. (currently amended): The compound of claim 1, wherein ~~X is  $NR^1R^2$ ; and U is~~ has the formula



~~wherein  $R^1$  and  $R^2$  are as defined in claim 1;~~

~~$R^3$  is H or  $C_{1-6}$ -alkyl;~~

~~n is 1-6; and~~

~~R<sup>4</sup> is H or a C<sub>1-10</sub> alkyl or C<sub>2-10</sub> alkenyl optionally containing one or more non-adjacent heteroatoms selected from N, O and S, and optionally substituted with a carbocyclic or heterocyclic ring; and~~

~~wherein R<sup>1</sup> and R<sup>2</sup> in NR<sup>1</sup>R<sup>2</sup>; and R<sup>3</sup> and R<sup>4</sup> in NR<sup>3</sup>R<sup>4</sup> each independently may form a substituted ring.~~

17. (currently amended): The compound of claim 16, wherein X is NR<sup>1</sup>R<sup>2</sup>, R<sup>1</sup> and R<sup>2</sup> together with N in NR<sup>1</sup>R<sup>2</sup> [[;]] and R<sup>3</sup> and R<sup>4</sup> together with N in NR<sup>3</sup>R<sup>4</sup> each independently form a substituted 5-6 membered ring containing one or more N, [[O or S]] O or S.

18. (original): The compound of claim 17, wherein X is optionally substituted with amino, carbamate, a C<sub>1-10</sub> alkyl containing one or more non-adjacent N, O or S, and optionally substituted with a heterocyclic ring; aryl or a saturated or unsaturated heterocyclic ring, each of which is optionally substituted.

19. (original): The compound of claim 17, wherein X is substituted with a heterocyclic ring selected from the group consisting of tetrahydrofuran, 1,3-dioxolane, 2,3-dihydrofuran, tetrahydropyran, benzofuran, isobenzofuran, 1,3-dihydro-isobenzofuran, isoxazole, 4,5-dihydroisoxazole, piperidine, pyrrolidine, pyrrolidin-2-one, pyrrole, pyridine, pyrimidine, octahydro-pyrrolo[3,4-*b*]pyridine, piperazine, pyrazine, morpholine, thiomorpholine, imidazole, imidazolidine-2,4-dione, benzimidazole, 1,3-dihydrobenzimidazol-2-one, indole, thiazole, benzothiazole, thiadiazole, thiophene, tetrahydro-thiophene 1,1-dioxide, diazepine, triazole, guanidine, diazabicyclo[2.2.1]heptane, 2,5-diazabicyclo[2.2.1]heptane, and 2,3,4,4a,9,9a-hexahydro-1H- $\beta$ -carboline.

20. (original): The compound of claim 17, wherein X and NR<sup>3</sup>R<sup>4</sup> are independently morpholine, thiomorpholine, imidazole, pyrrolidine, piperazine, pyridine or piperidine.

21. (original): The compound of claim 20, wherein X and NR<sup>3</sup>R<sup>4</sup> are independently pyrrolidine.

22. (original): The compound of claim 21, wherein X is substituted with pyrazine.
23. (original): The compound of claim 22, wherein W is naphthalenyl.
24. (original): The compound of claim 1, wherein W is benzene, pyridine, biphenyl, naphthalene, phenanthrene, quinoline, isoquinoline, quinazoline, cinnoline, phthalazine, quinoxaline, indole, benzimidazole, benzoxazole, benzthiazole, benzofuran, anthrone, xanthone, acridone, fluorenone, carbazolyl, pyrimido[4,3-*b*]furan, pyrido[4,3-*b*]indole, pyrido[2,3-*b*]indole, dibenzofuran, acridine or acridizine.
- 25-26. (canceled)
27. (original): The compound of claim 1, wherein said compound is chiral.
28. (original): A pharmaceutical composition comprising the compound of claim 1 and a pharmaceutically acceptable excipient.
29. (withdrawn): A method for ameliorating a cell proliferative disorder, comprising administering to a subject in need thereof an effective amount of the compound of claim 1 or a pharmaceutical composition thereof, thereby ameliorating said cell-proliferative disorder.
30. (withdrawn): The method of claim 29, wherein said cell proliferative disorder is cancer.
31. (withdrawn): The method of claim 29, wherein cell proliferation is reduced, or cell death is induced.
32. (withdrawn): The method of claim 29, wherein said subject is human or an animal.

33. (withdrawn): A method for reducing cell proliferation or inducing cell death, comprising contacting a system with an effective amount of the compound of claim 1 or a pharmaceutical composition thereof, thereby reducing cell proliferation or inducing cell death in said system.

34. (withdrawn): The method of claim 33, wherein said system is a cell or tissue.

35. (withdrawn): A method for reducing microbial titers, comprising contacting a system with an effective amount of the compound of claim 1 or a pharmaceutical composition thereof, thereby reducing microbial titers.

36. (withdrawn): The method of claim 35, where the system is a cell or tissue.

37. (withdrawn): The method of claim 35, wherein the microbial titers are viral, bacterial or fungal titers.

38. (withdrawn): A method for ameliorating a microbial infection, comprising administering to a subject in need thereof an effective amount of the compound of claim 1 or a pharmaceutical composition thereof, thereby ameliorating said microbial infection.

39. (withdrawn): The method of claim 38, where the subject is a human or an animal.

40. (withdrawn): The method of claim 38, wherein said microbial infection is viral, bacterial or fungal.

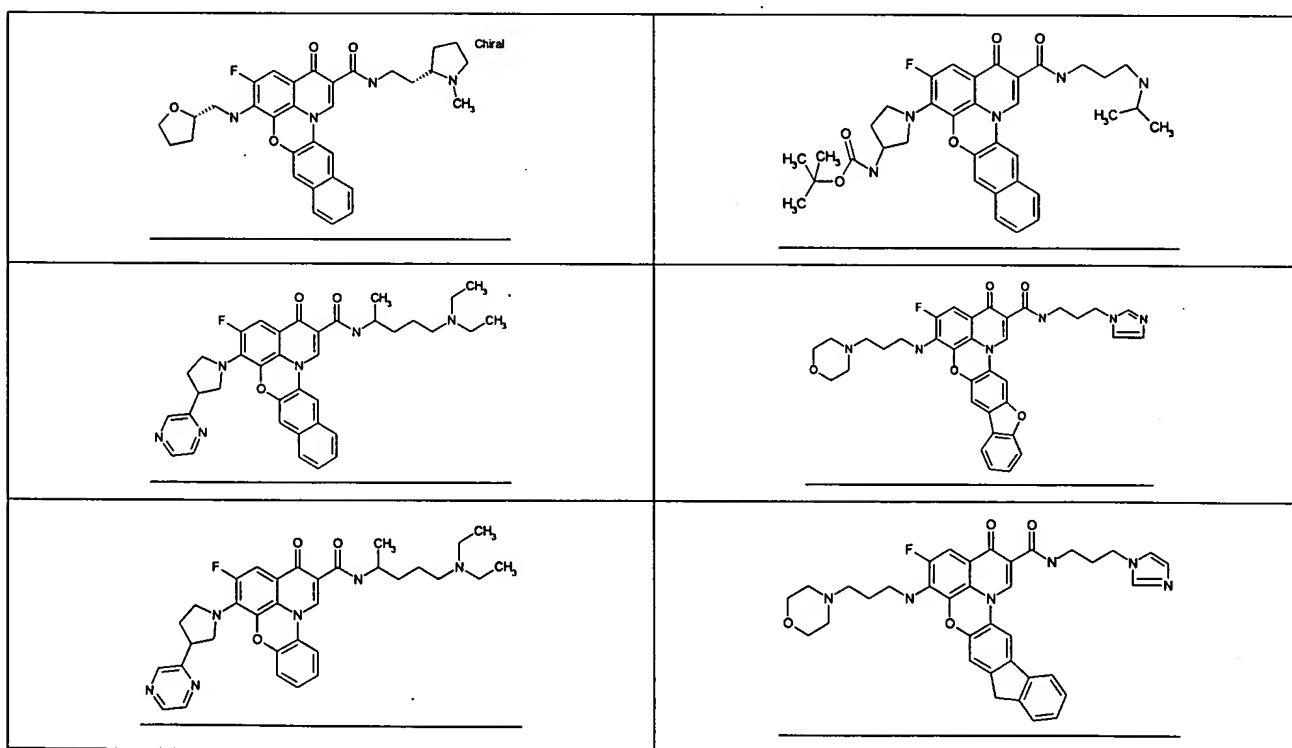
41. (currently amended): The compound of claim 1, wherein V is H or NH<sub>2</sub> or NR<sup>1</sup>—(CR<sub>2</sub><sup>+</sup>)<sub>n</sub>—NR<sup>3</sup>R<sup>4</sup>;  
wherein R<sup>1</sup> and R<sup>3</sup> are independently H or C<sub>1-6</sub>-alkyl;

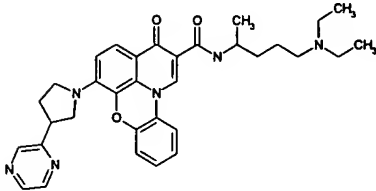
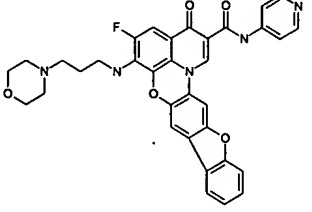
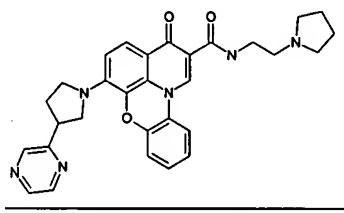
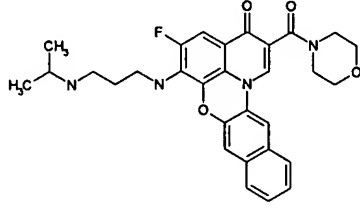
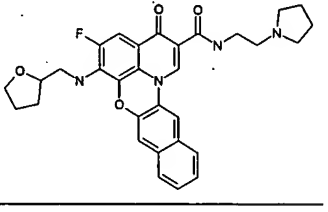
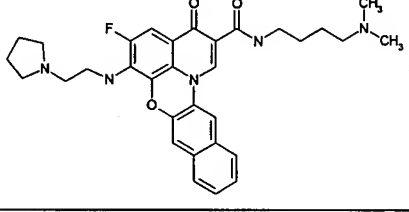
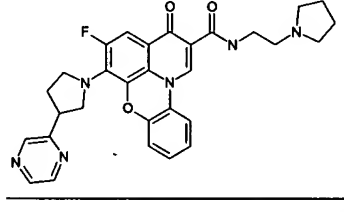
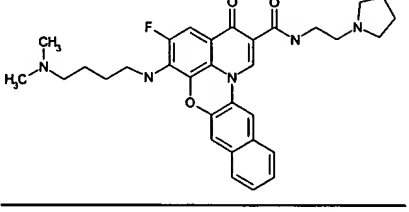
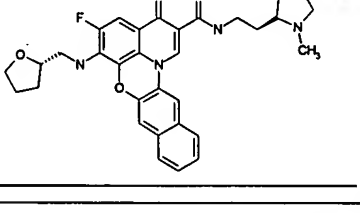
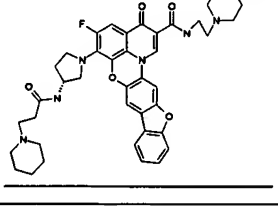
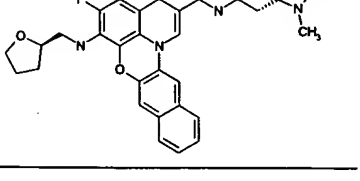


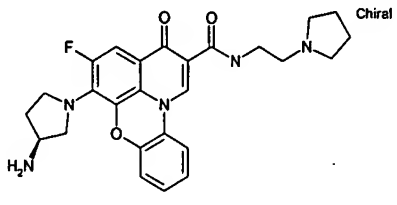
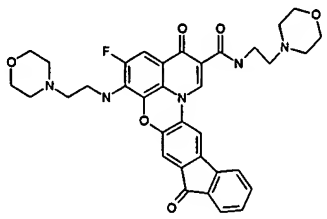
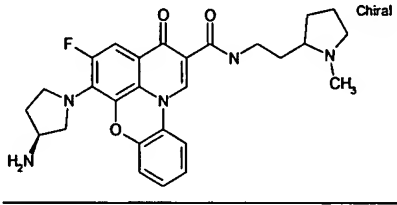
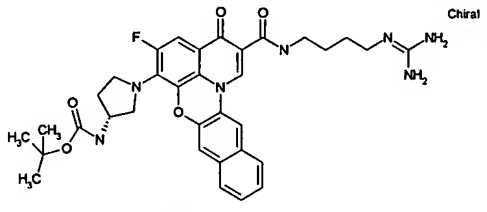
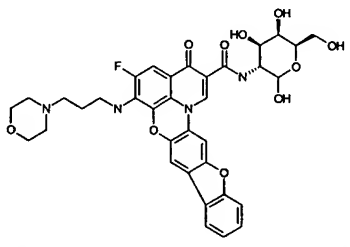
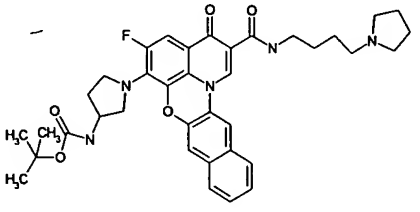
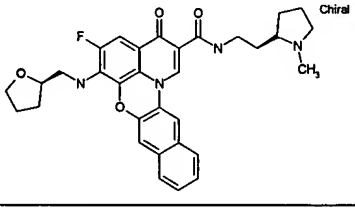
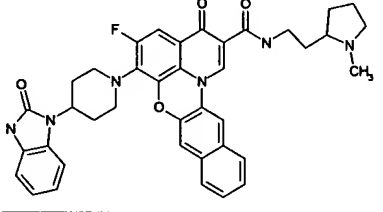
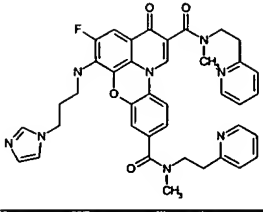
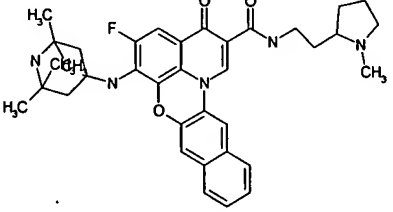
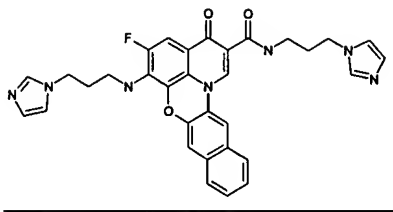
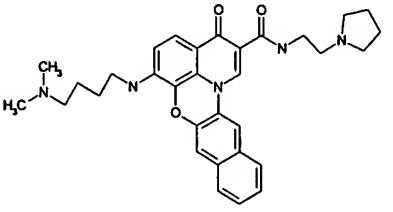
~~n is 1-6; and~~

~~R<sup>4</sup> is H, C<sub>1-6</sub>-alkyl optionally substituted with a carbocyclic or heterocyclic ring, or aryl; and  
wherein R<sup>3</sup> and R<sup>4</sup> in NR<sup>3</sup>R<sup>4</sup> may form an optionally substituted ring.~~

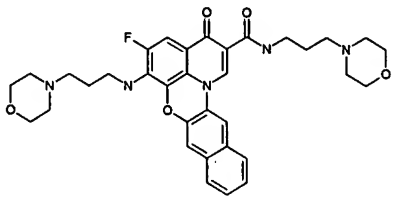
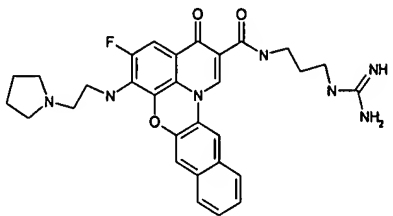
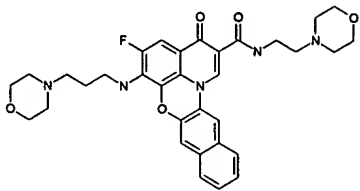
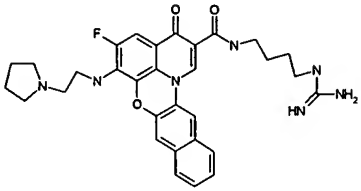
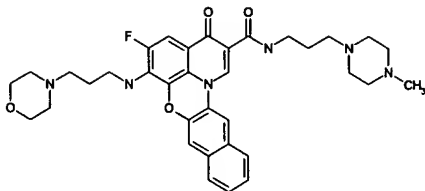
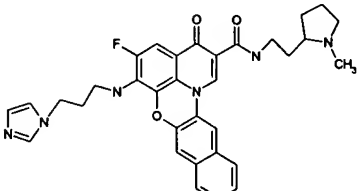
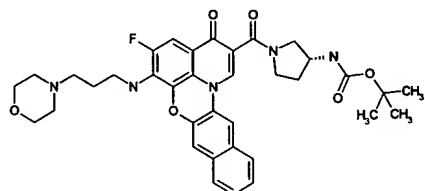
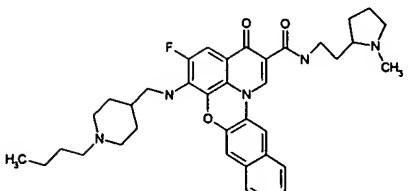
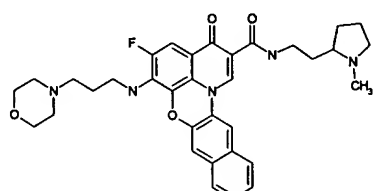
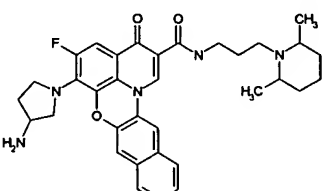
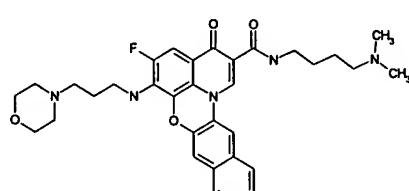
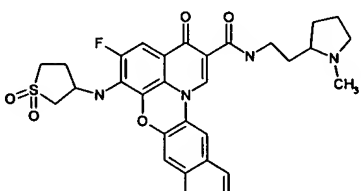
42. (original): The compound of claim 16, wherein V is H.
43. (original): The compound of claim 16, wherein A is fluoro.
44. (original): The compound of claim 16, wherein W is naphthalenyl.
45. (original): The compound of claim 23, wherein V is H and A is fluoro.
46. (currently amended): The compound of claim 1, wherein said compound is selected from the compounds in Figure 1.

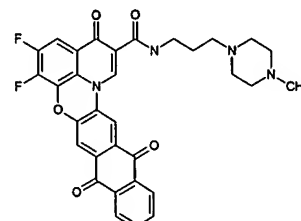
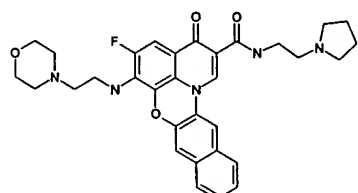
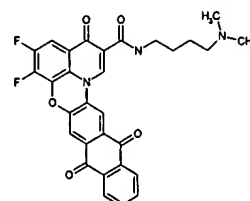
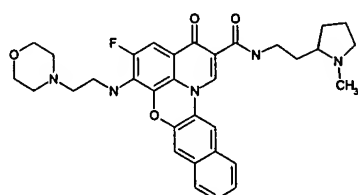
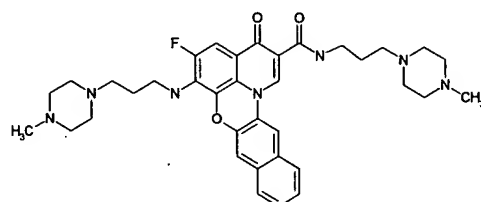
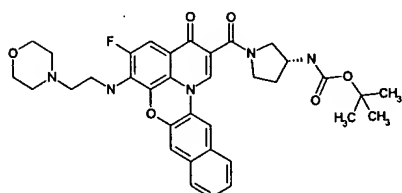
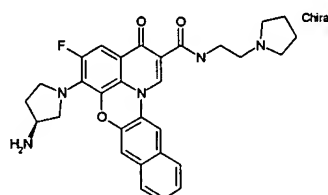
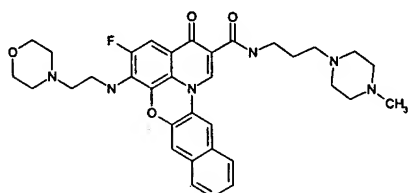
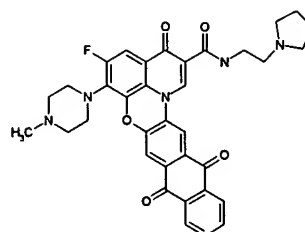
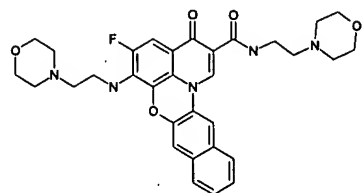
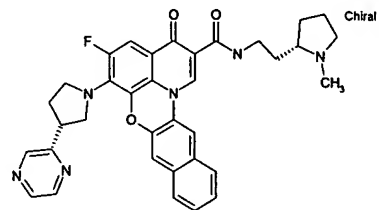
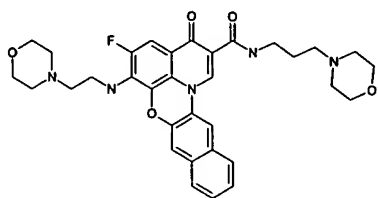


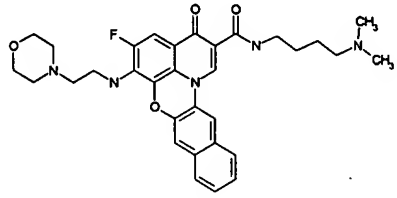
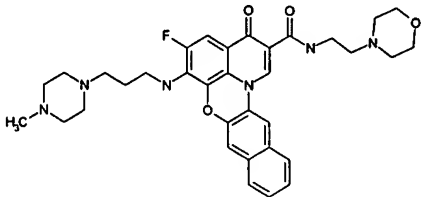
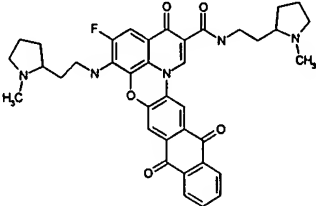
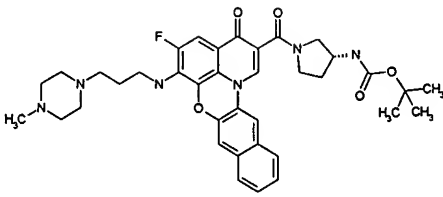
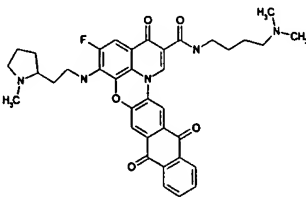
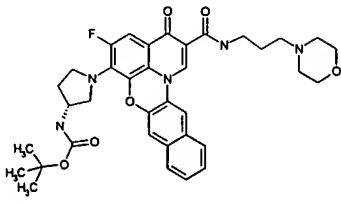
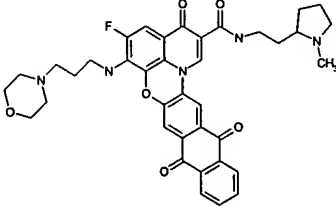
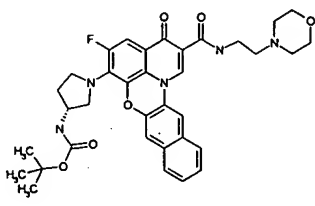
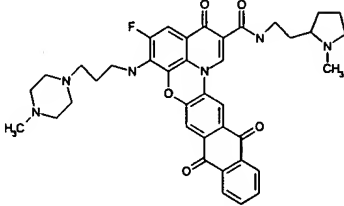
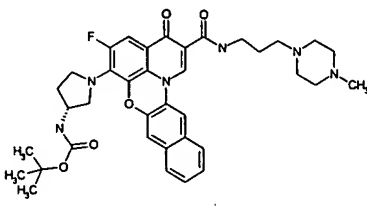
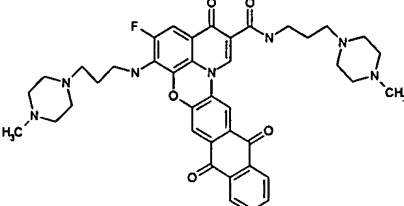
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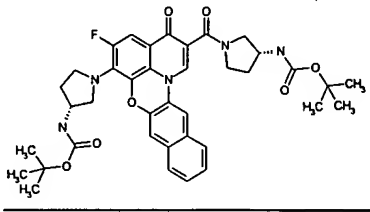
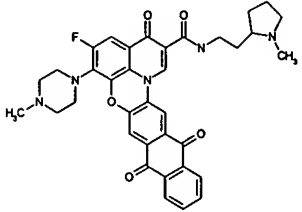
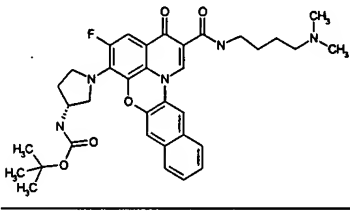
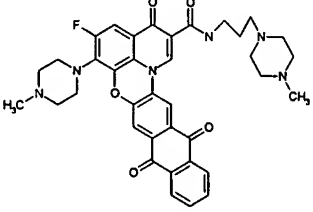
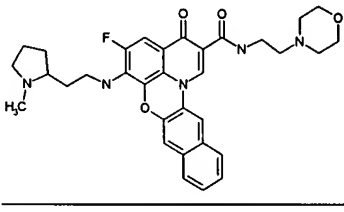
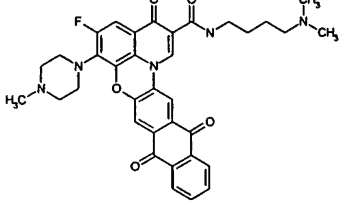
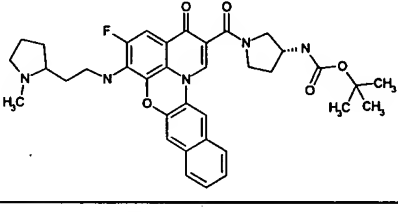
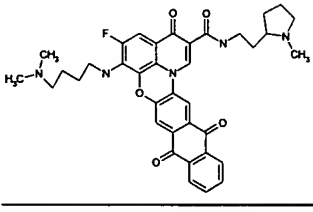
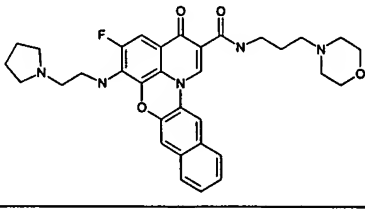
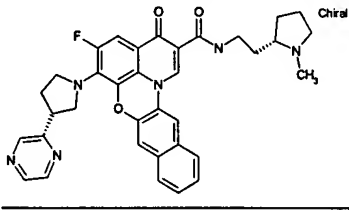
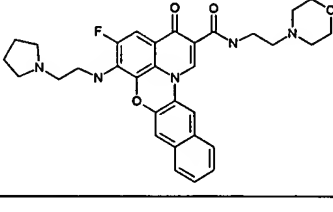
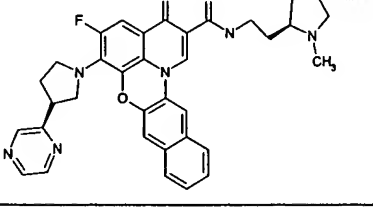
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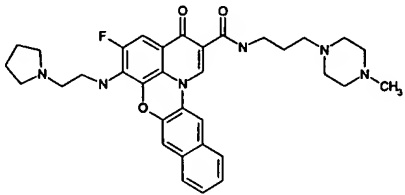
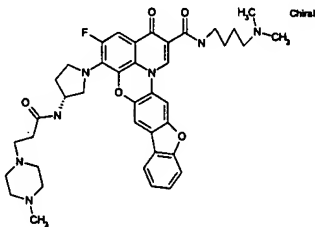
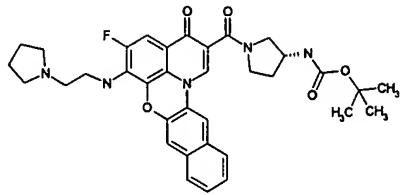
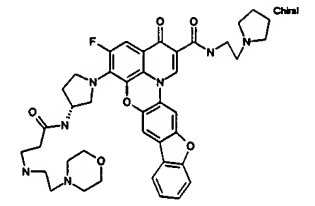
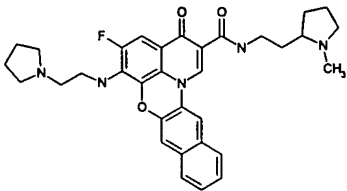
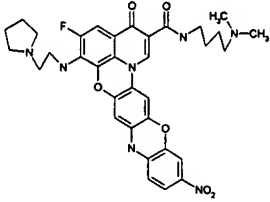
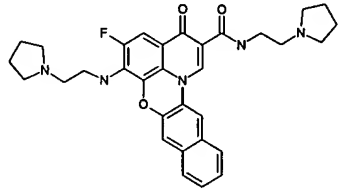
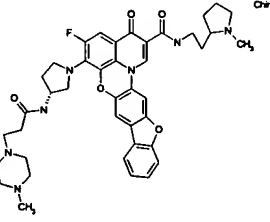
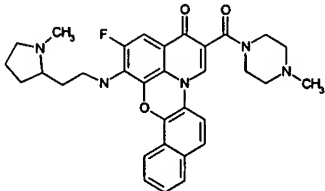
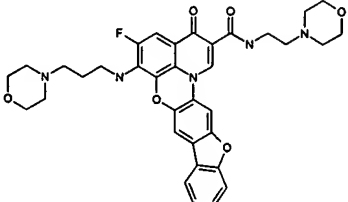
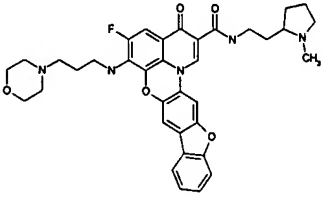
	
	
	
	
	
	

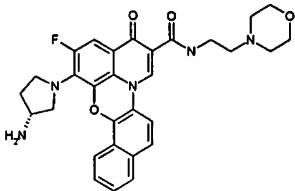
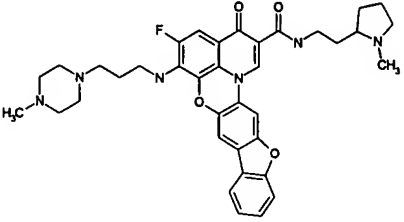
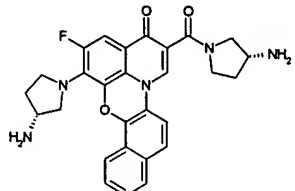
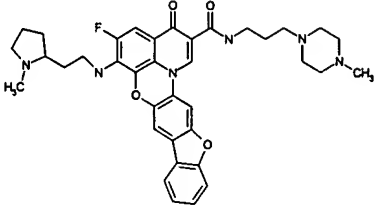
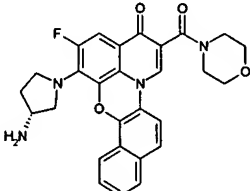
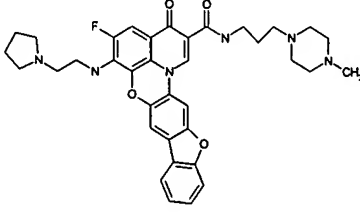
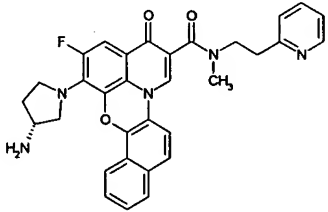
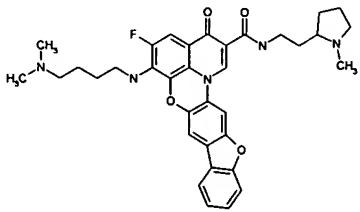
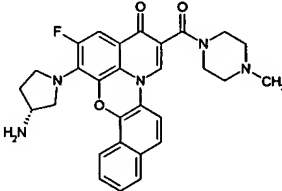
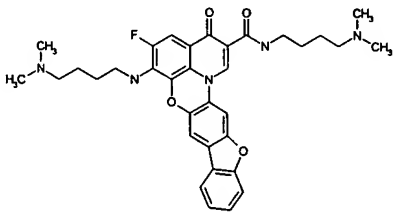
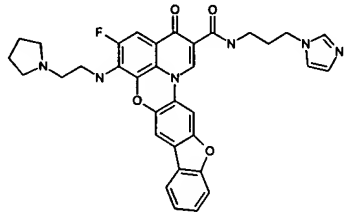


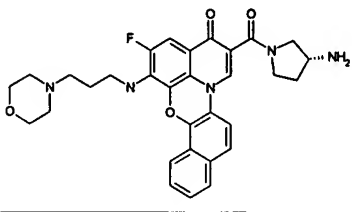
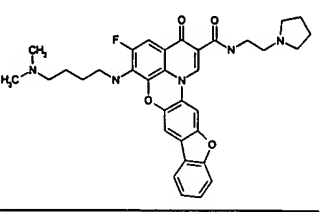
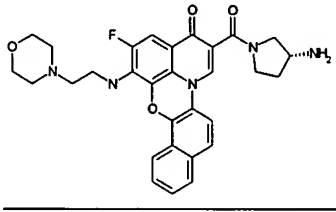
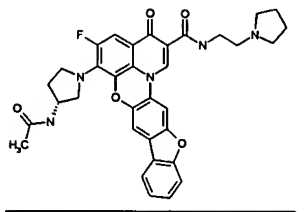
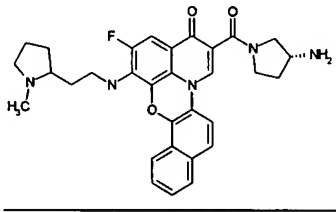
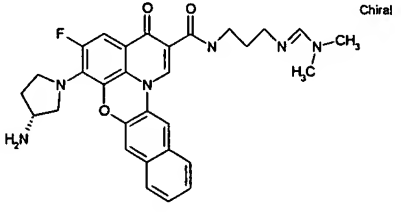
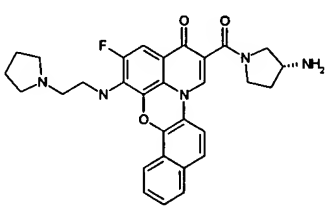
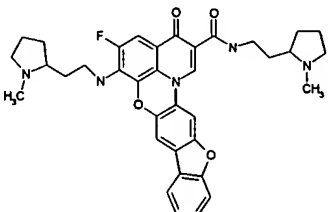
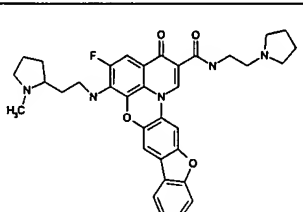
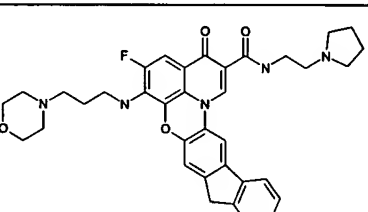
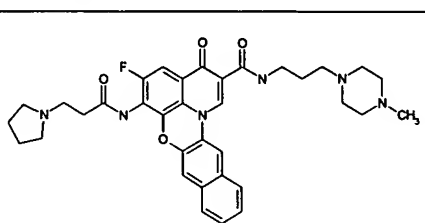
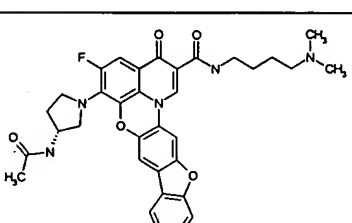
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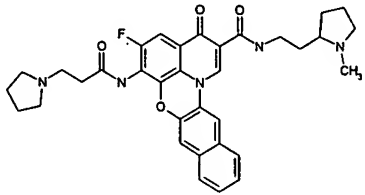
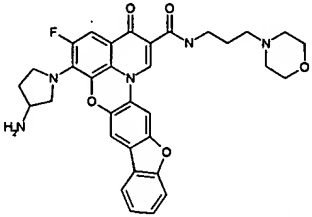
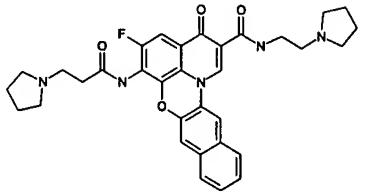
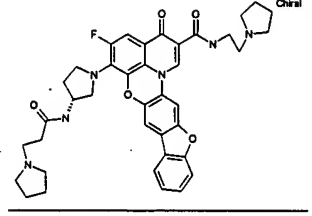
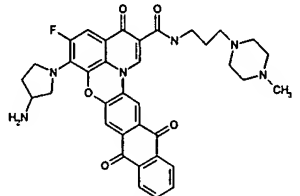
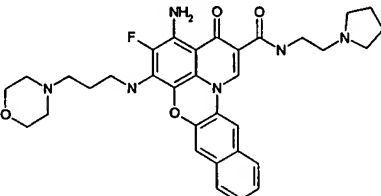
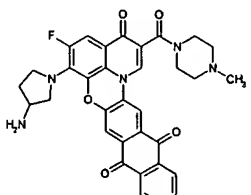
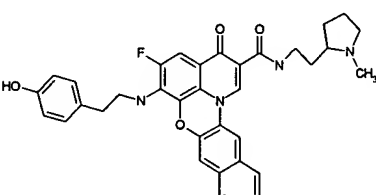
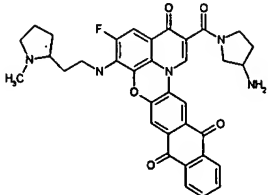
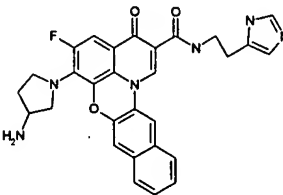
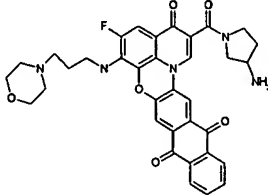
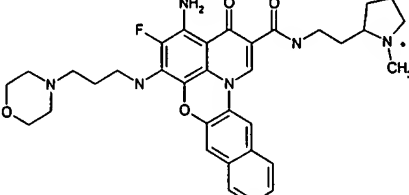
	
	
	
	
	
	

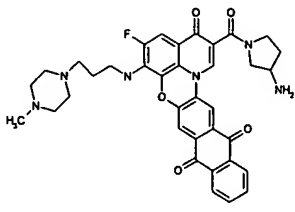
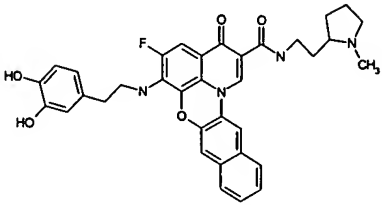
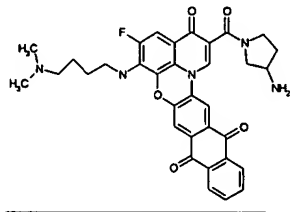
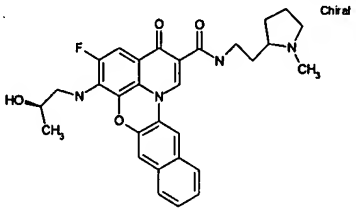
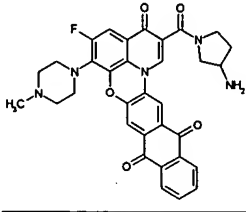
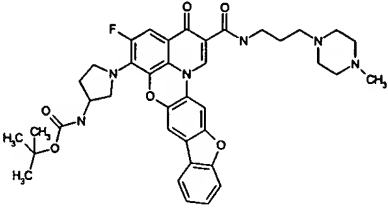
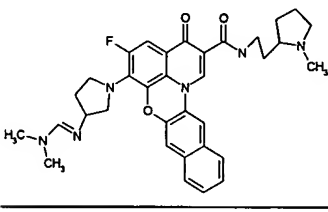
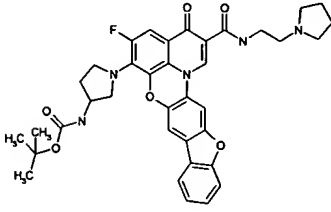
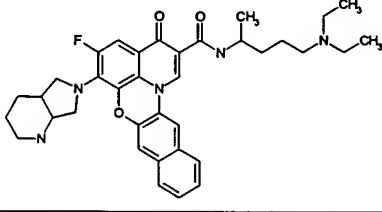
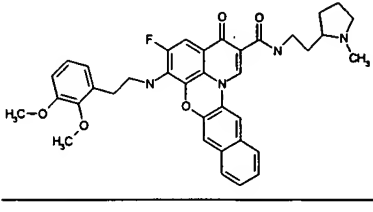
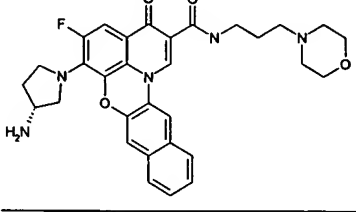


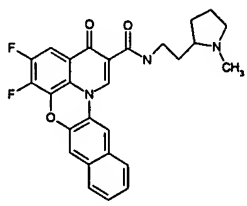
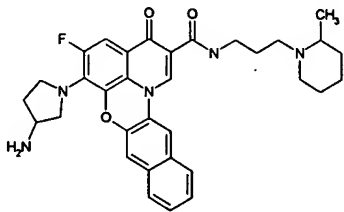
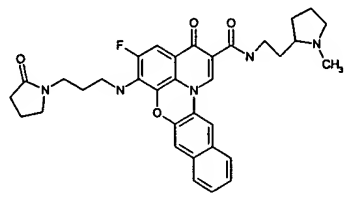
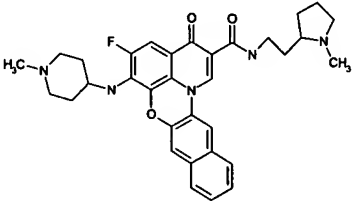
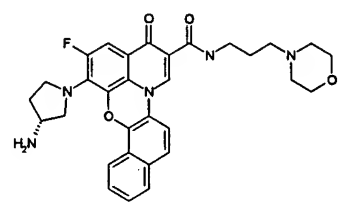
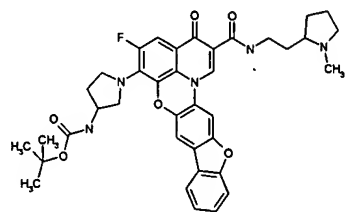
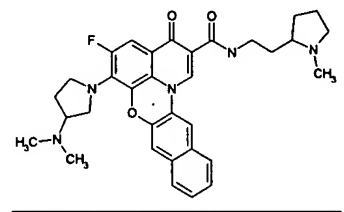
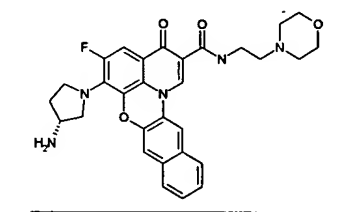
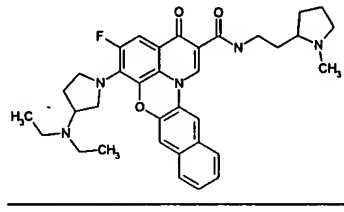
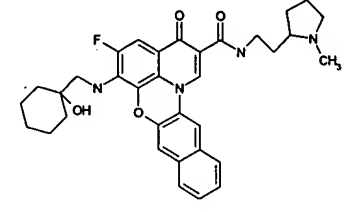
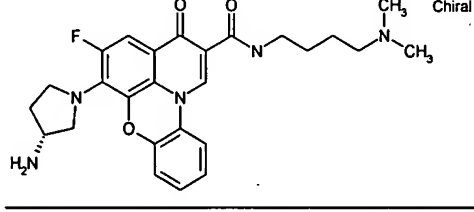
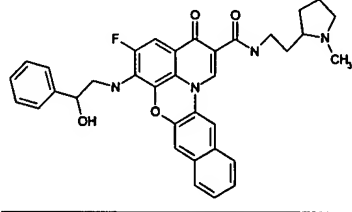
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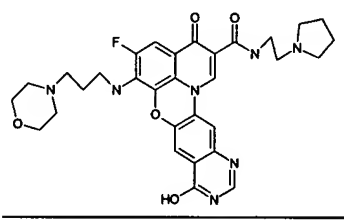
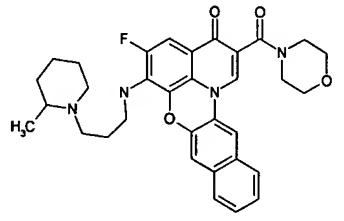
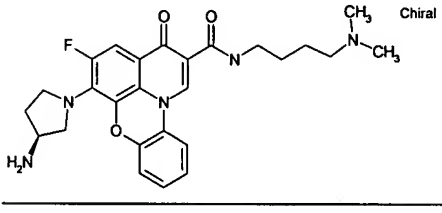
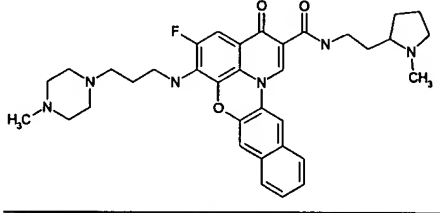
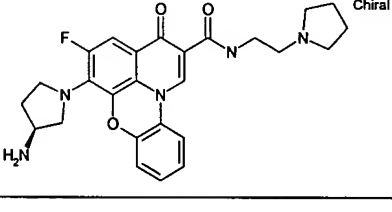
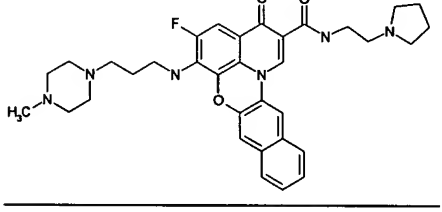
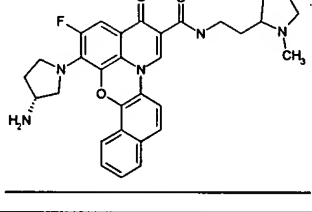
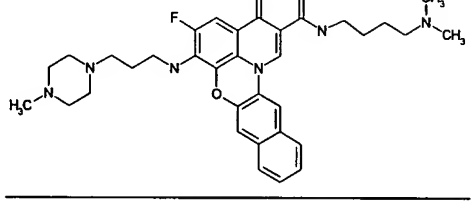
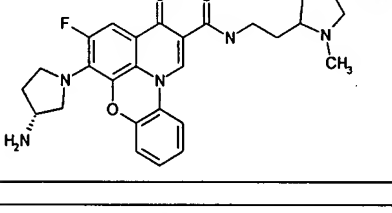
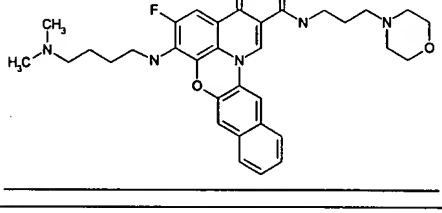
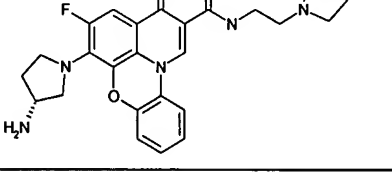
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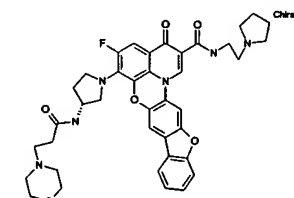
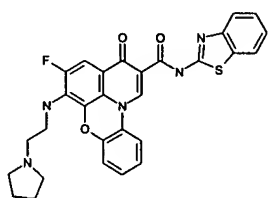
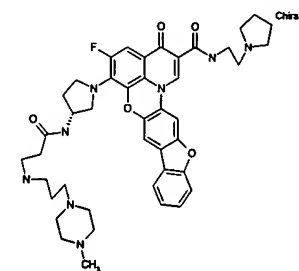
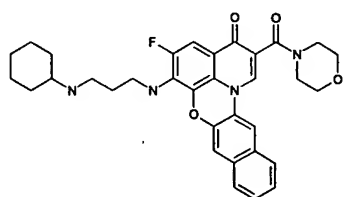
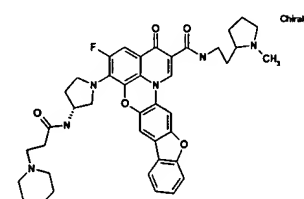
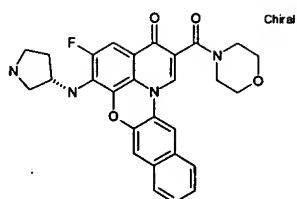
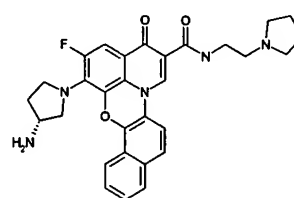
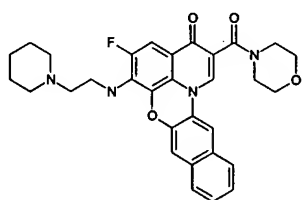
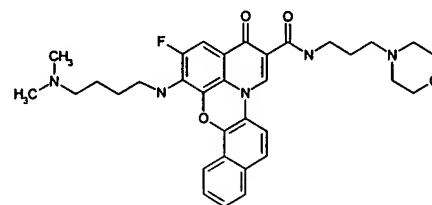
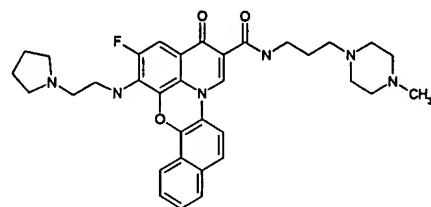
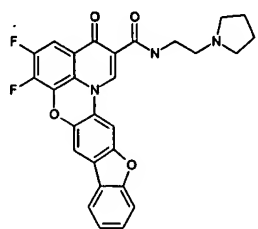
	
	
	
	
	
	

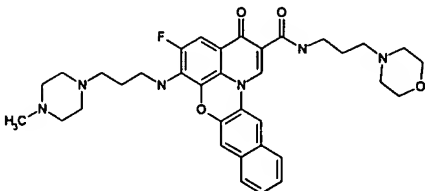
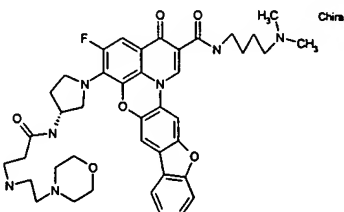
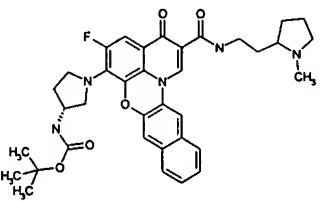
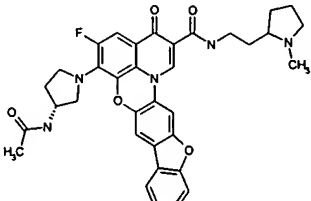
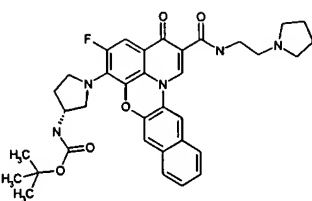
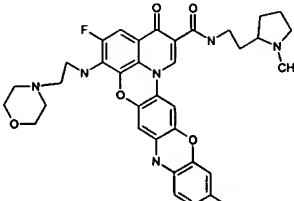
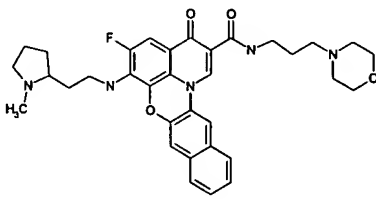
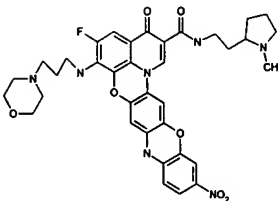
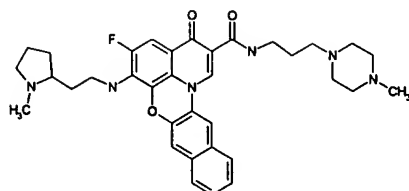
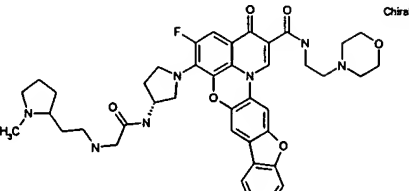
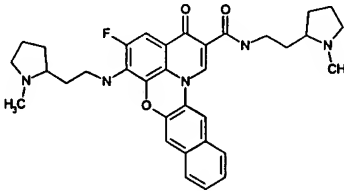
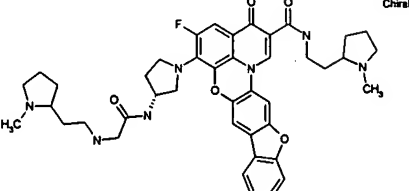
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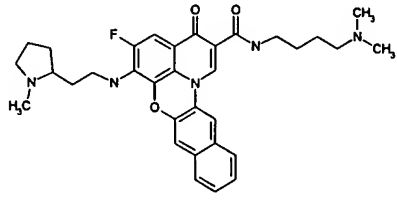
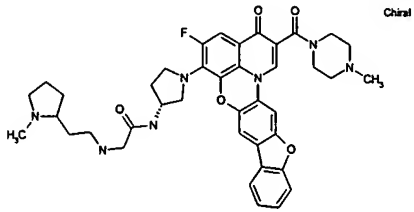
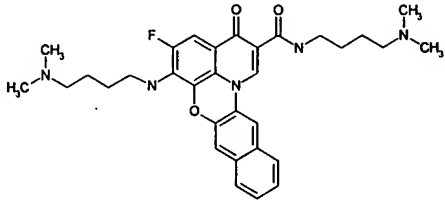
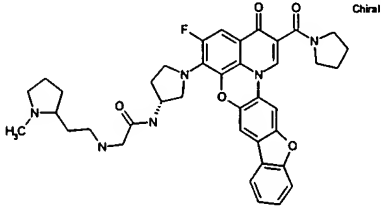
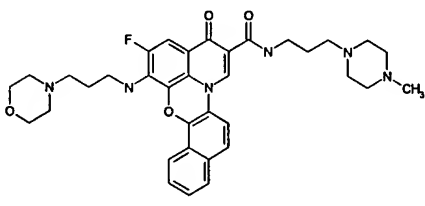
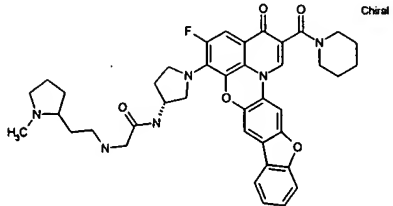
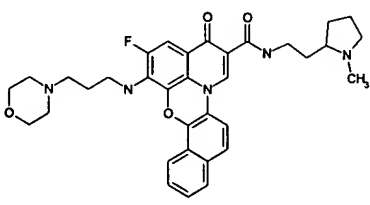
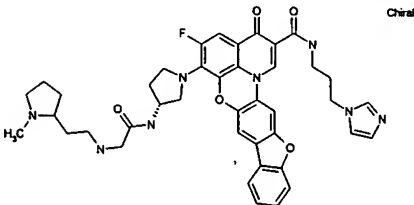
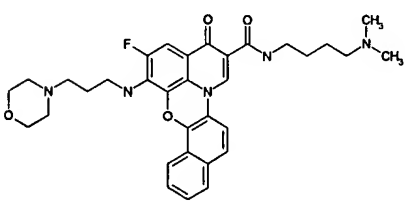
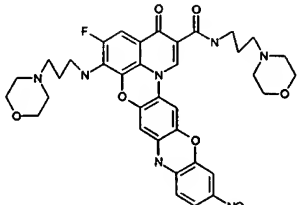
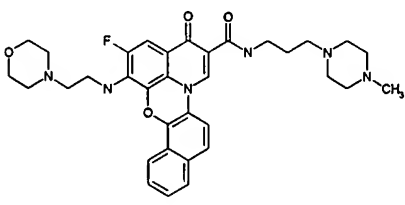
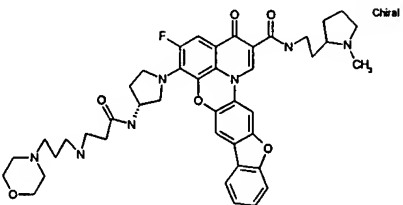
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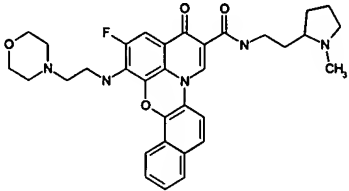
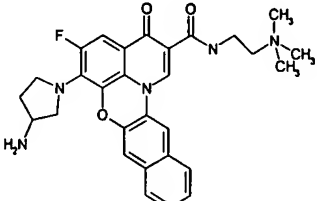
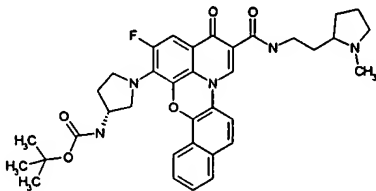
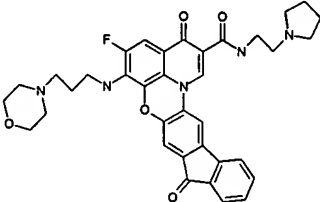
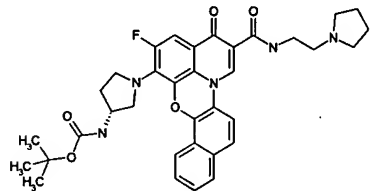
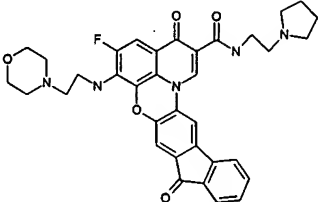
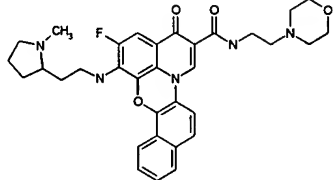
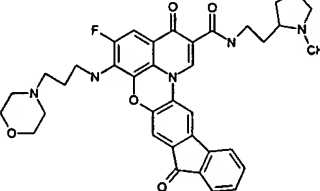
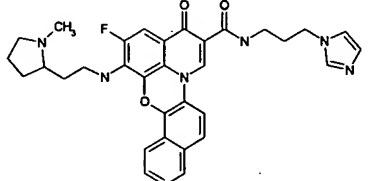
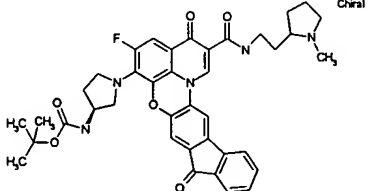
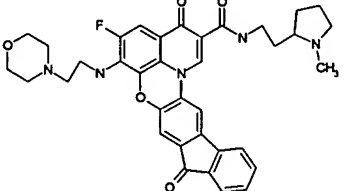
	
	
	
	
	
	

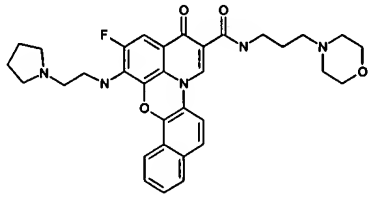
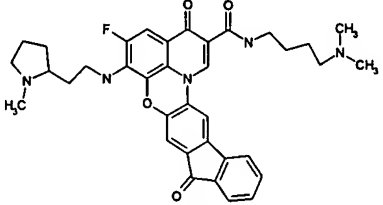
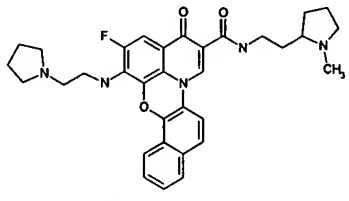
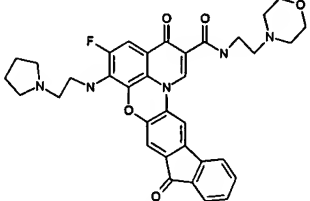
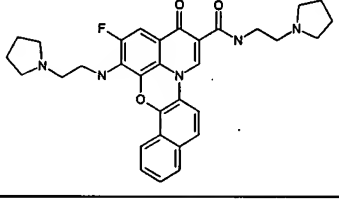
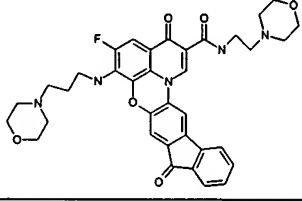
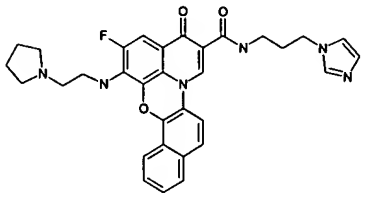
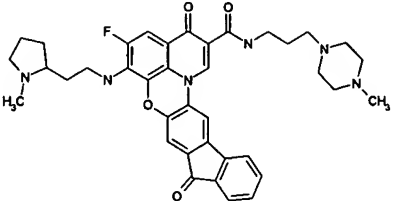
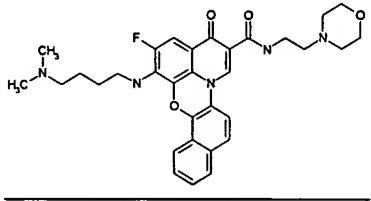
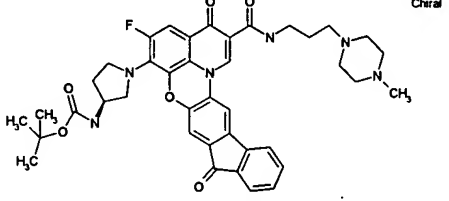
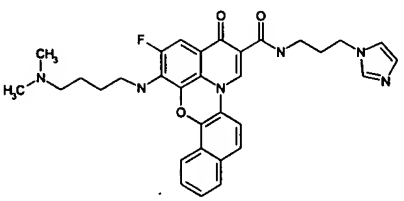
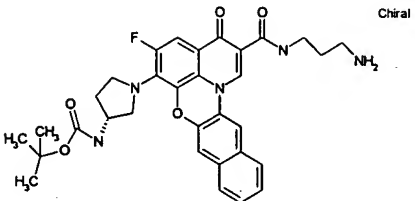


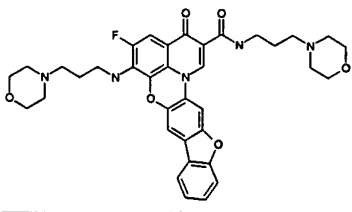
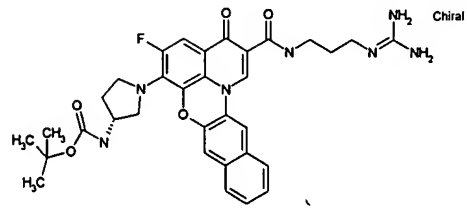
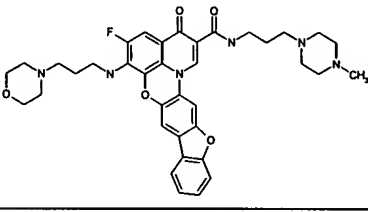
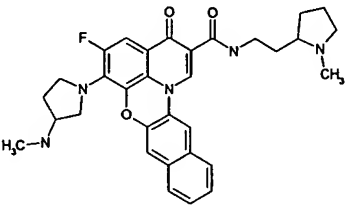
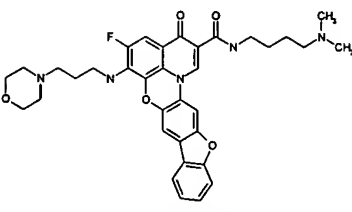
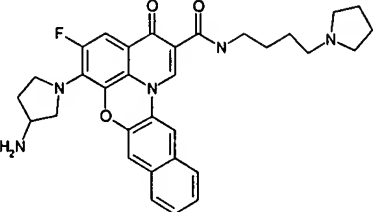
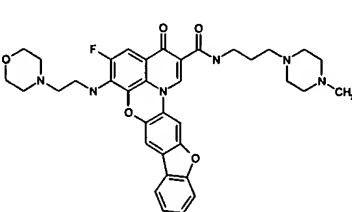
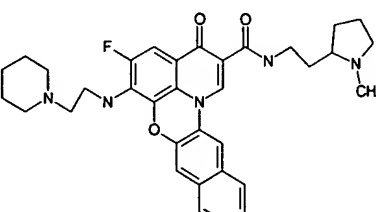
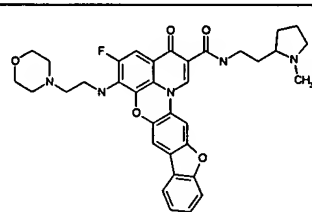
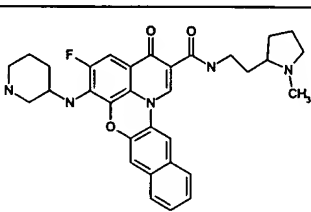
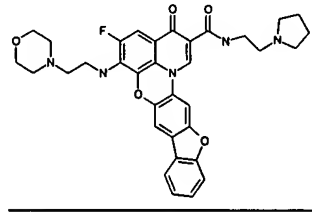
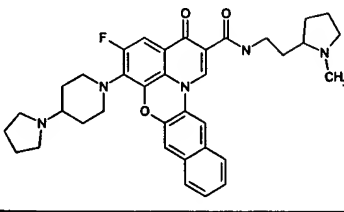


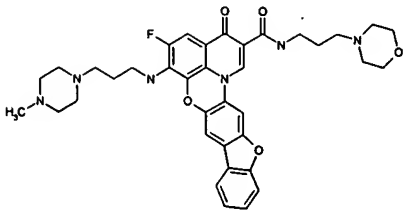
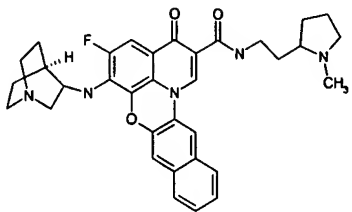
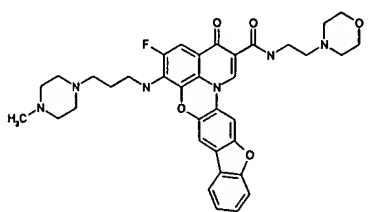
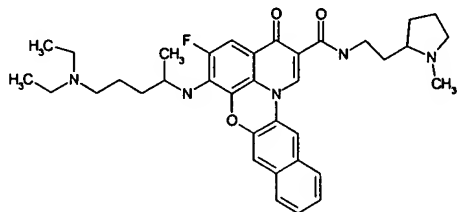
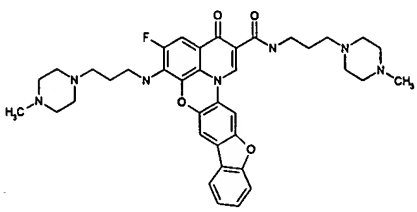
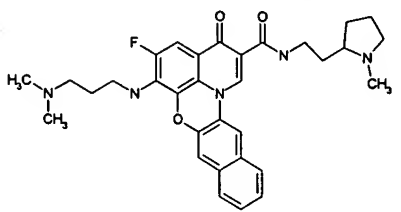
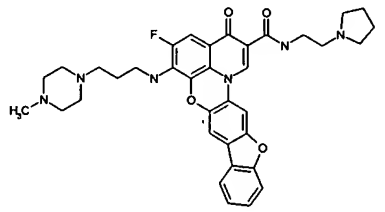
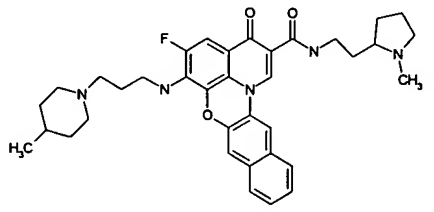
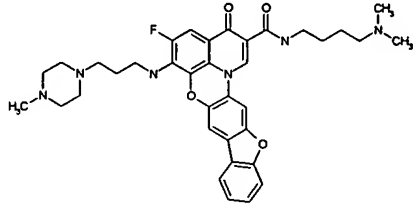
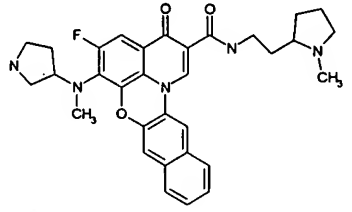
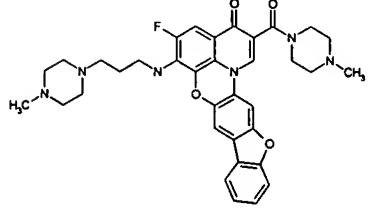
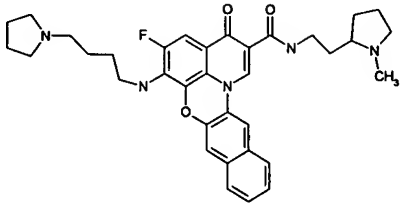
	
	
	
	
	
	

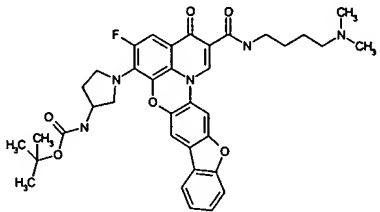
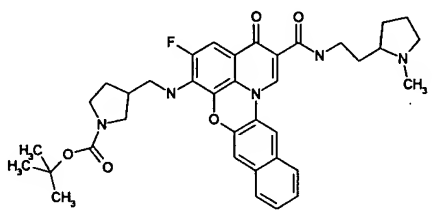
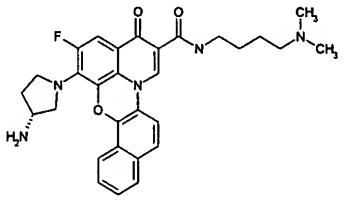
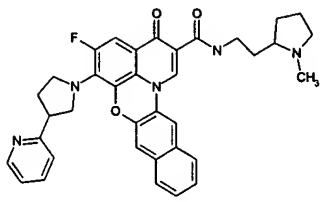
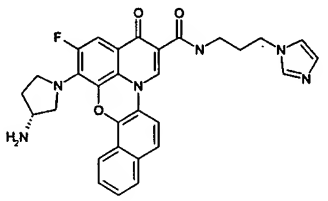
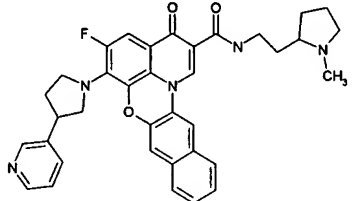
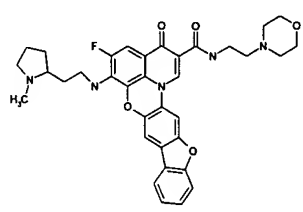
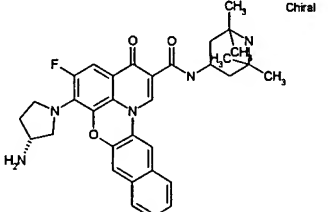
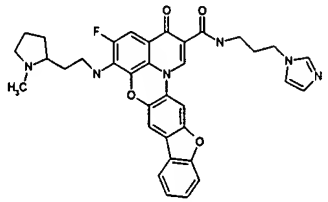
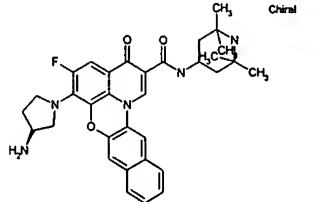
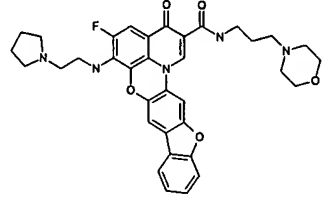
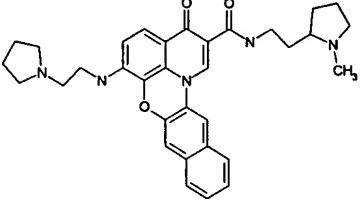
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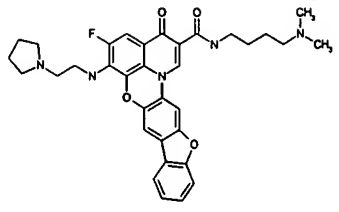
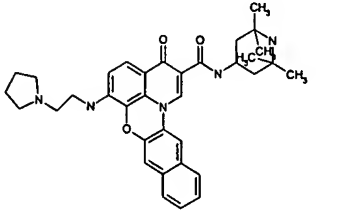
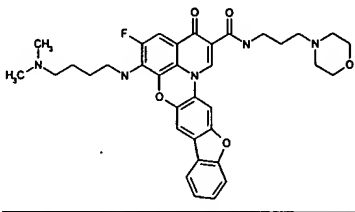
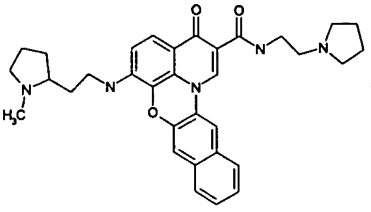
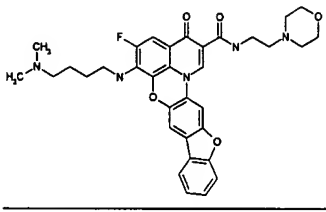
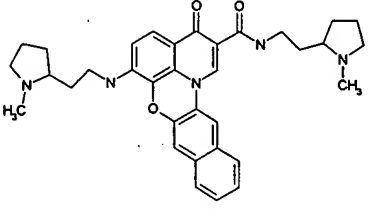
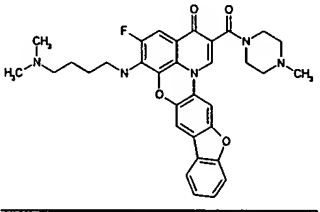
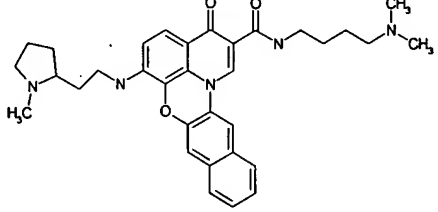
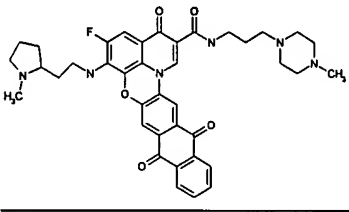
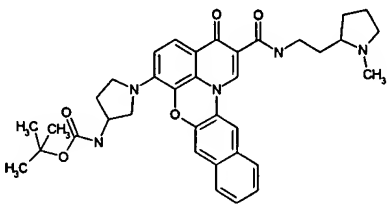
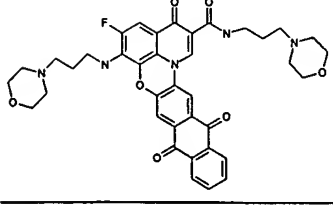
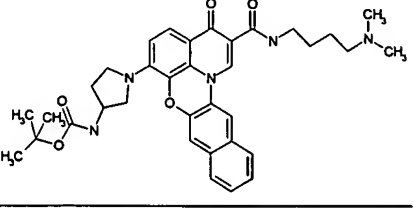
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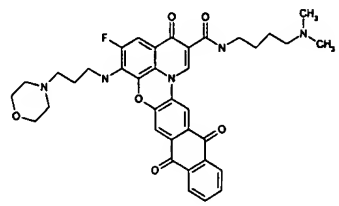
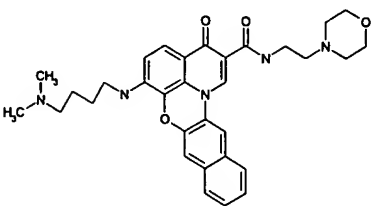
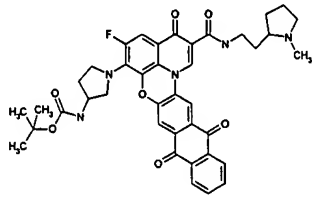
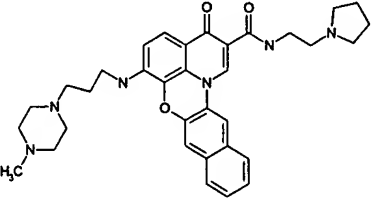
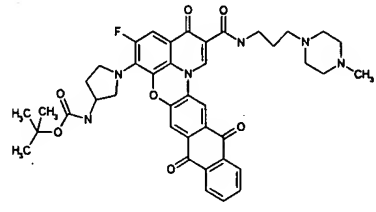
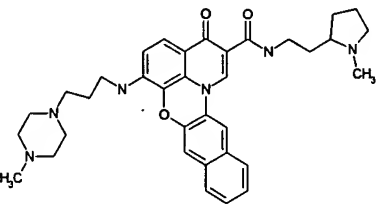
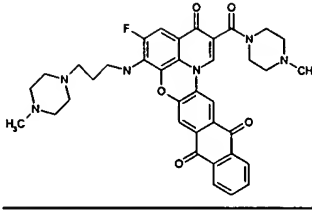
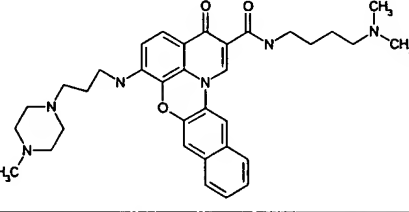
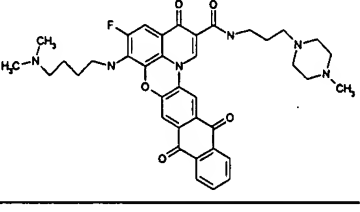
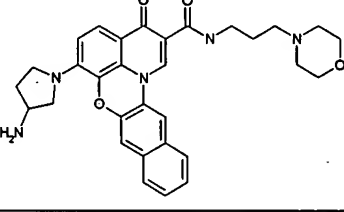
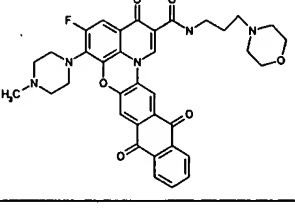
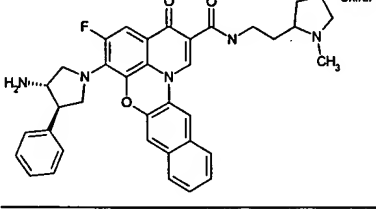
	
	
	
	
	
	

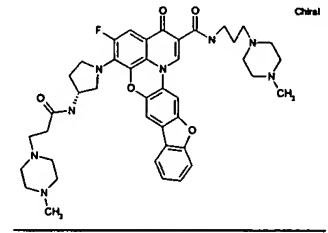
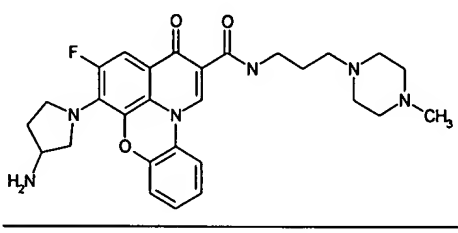
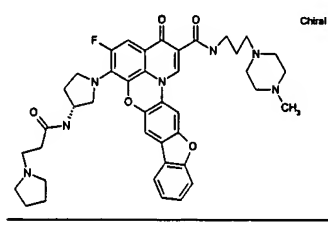
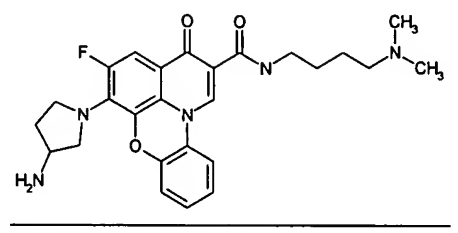
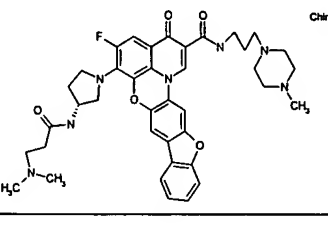
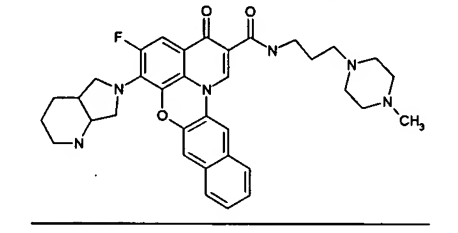
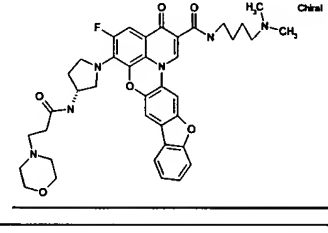
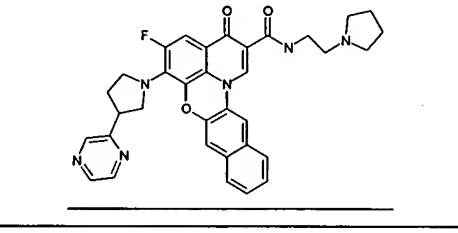
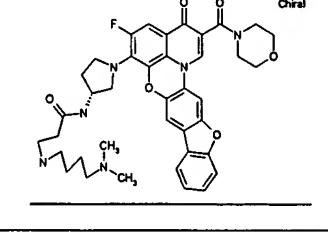
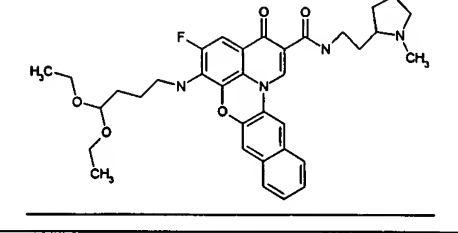
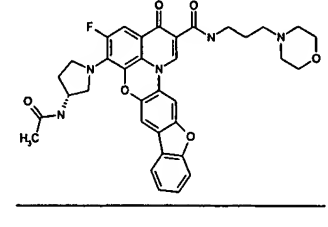
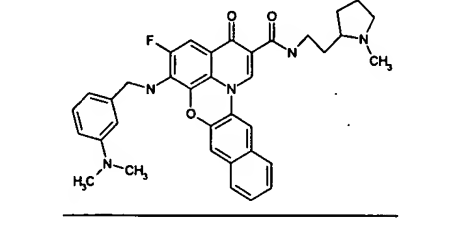
	
	
	
	
	
	

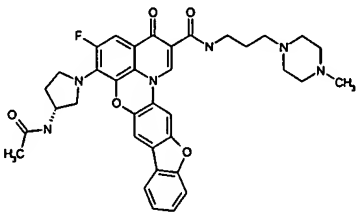
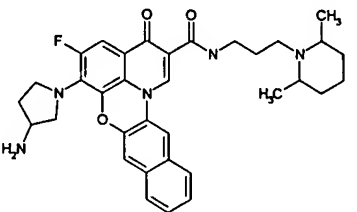
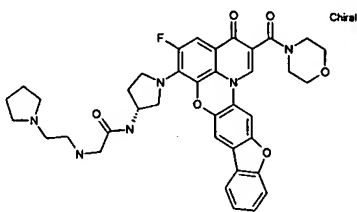
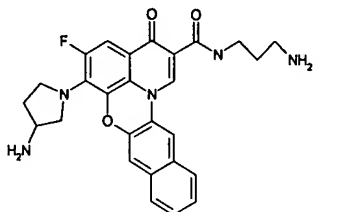
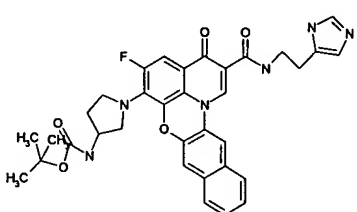
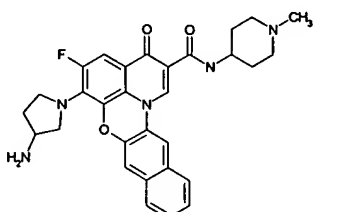
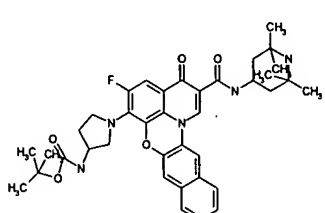
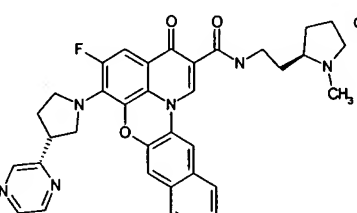
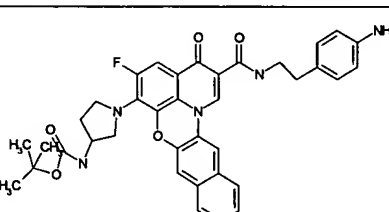
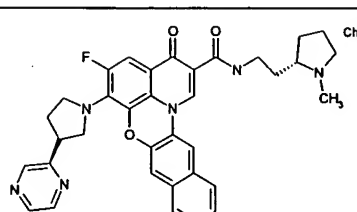
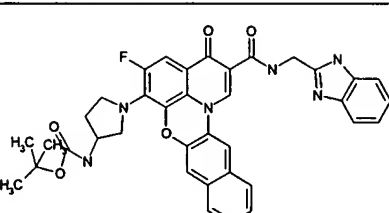
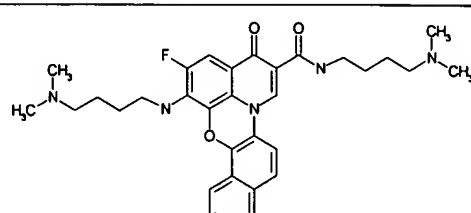
	
	
	
	
	
	

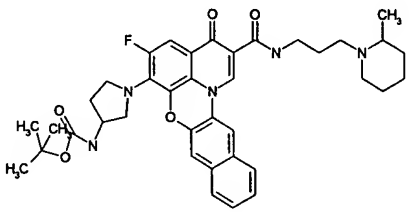
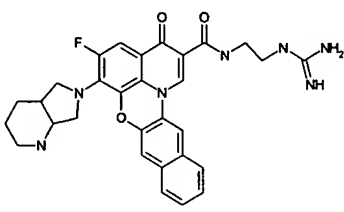
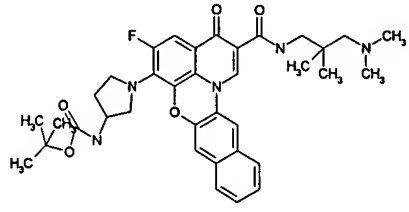
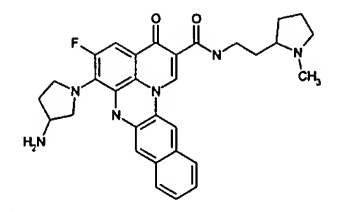
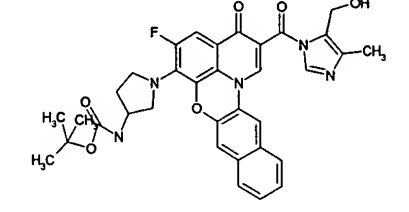
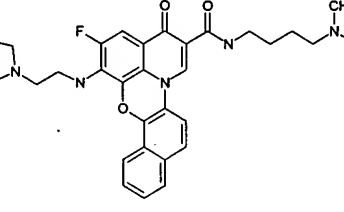
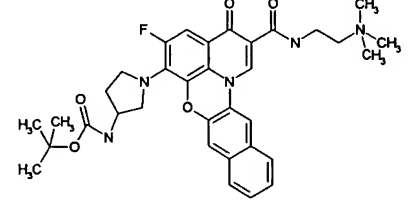
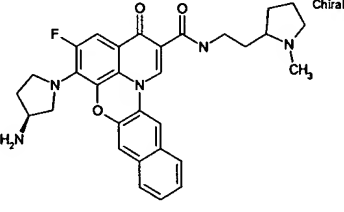
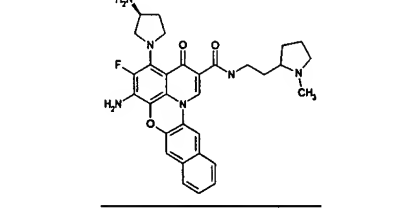
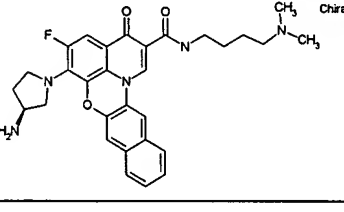
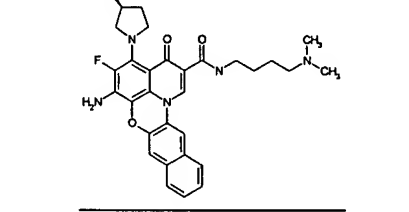
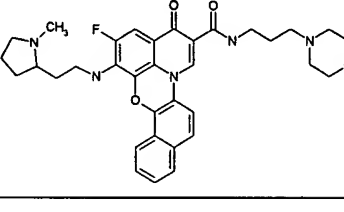
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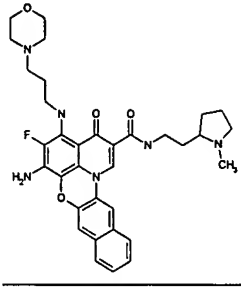
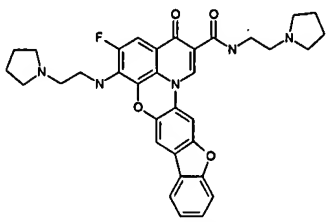
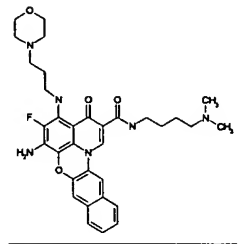
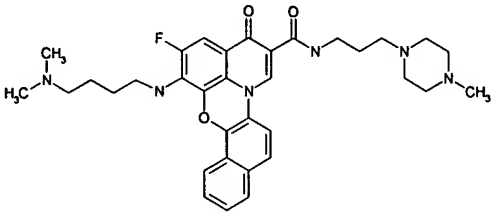
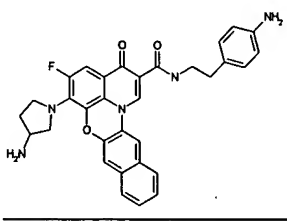
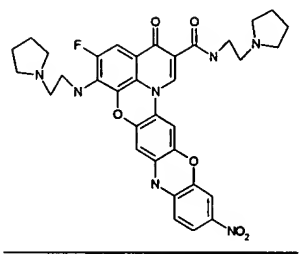
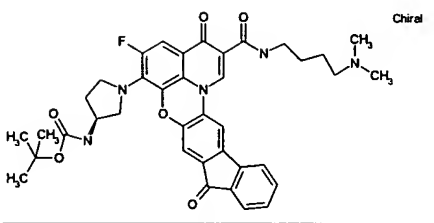
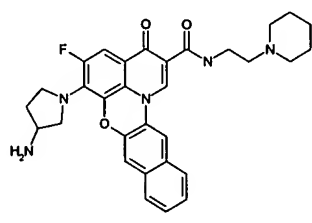
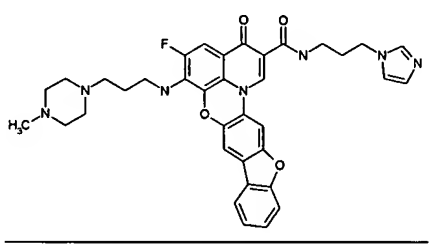


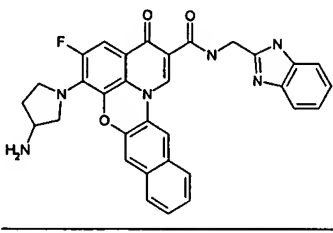
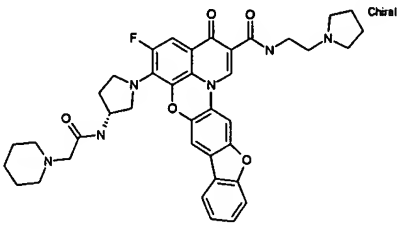
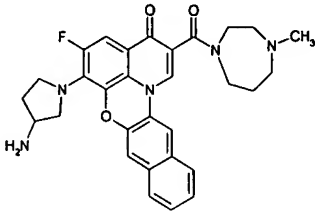
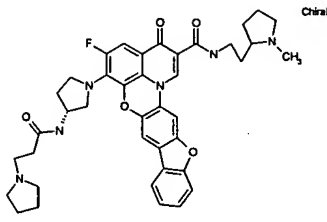
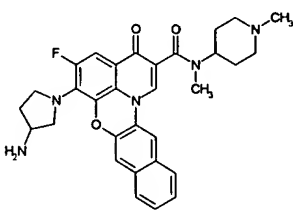
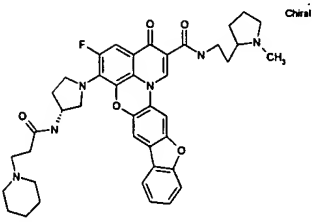
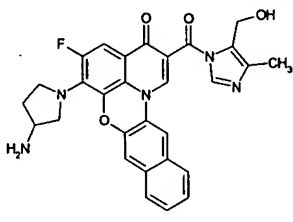
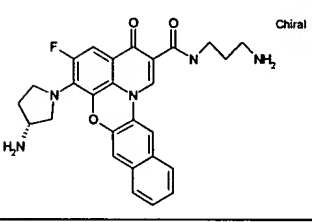
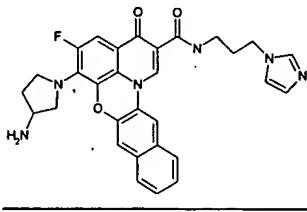
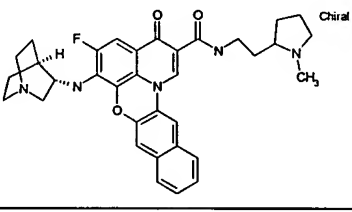
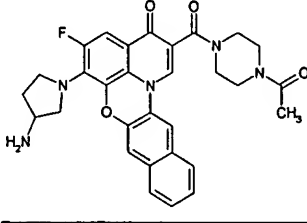
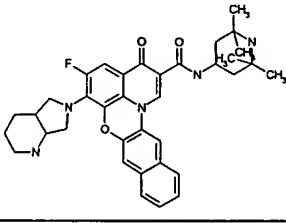
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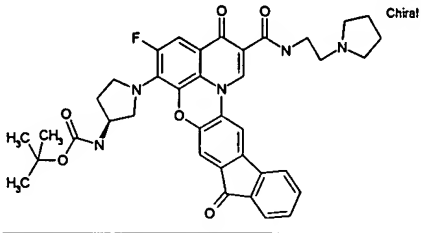
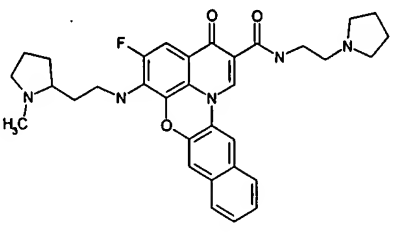
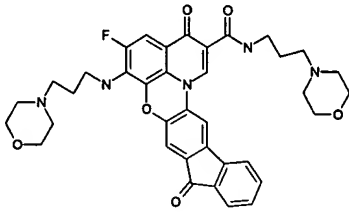
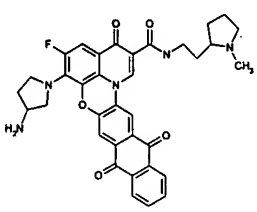
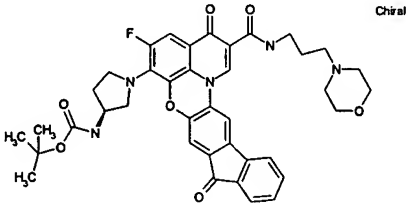
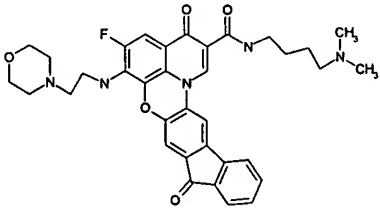
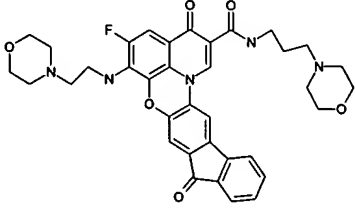
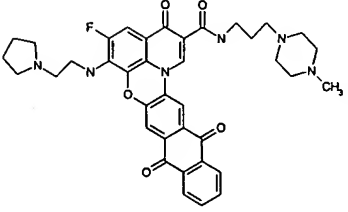
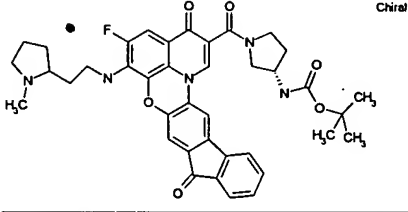
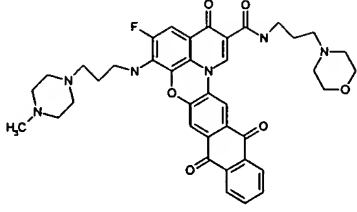
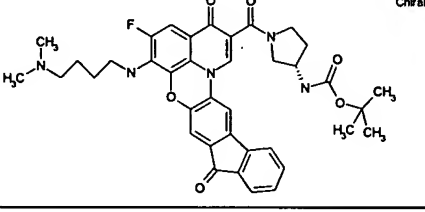
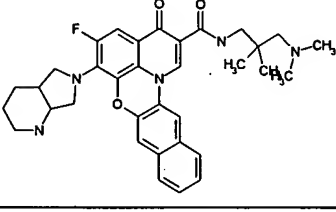
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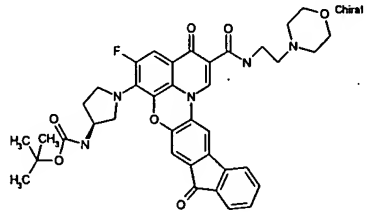
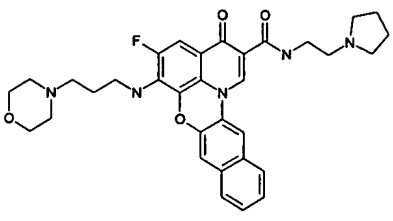
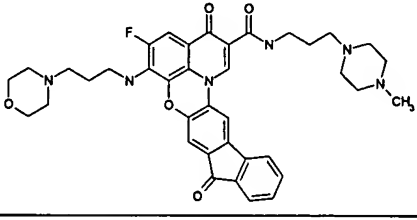
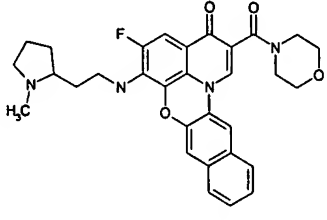
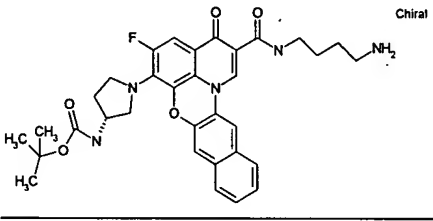
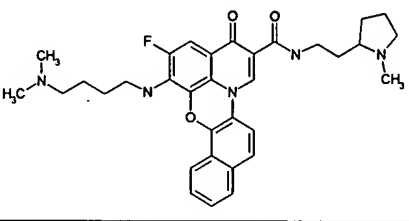
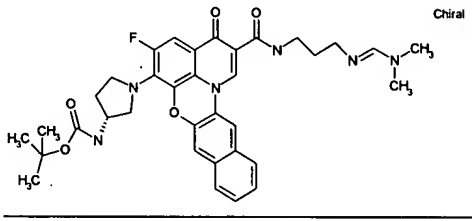
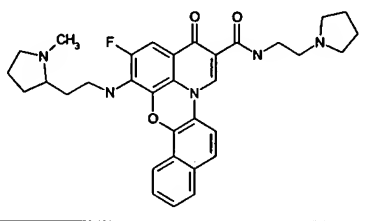
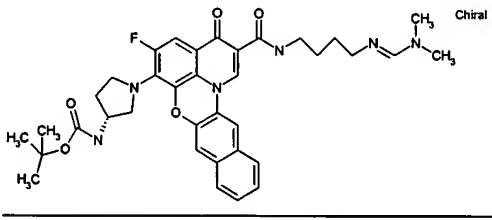
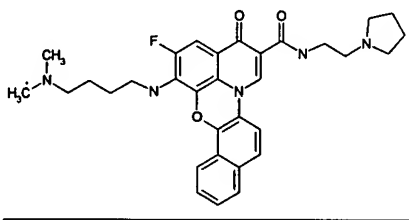
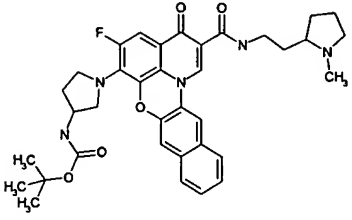
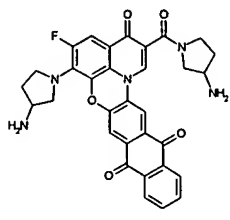
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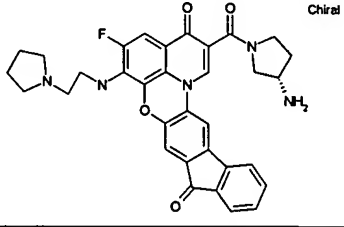
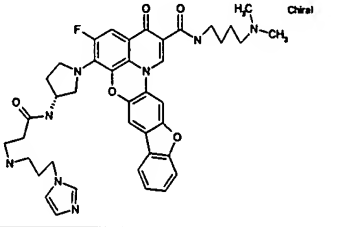
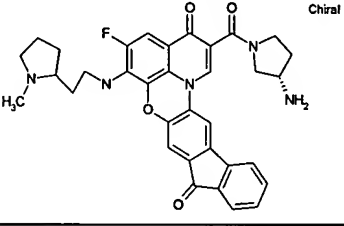
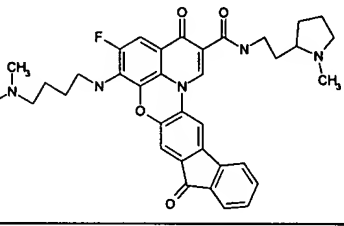
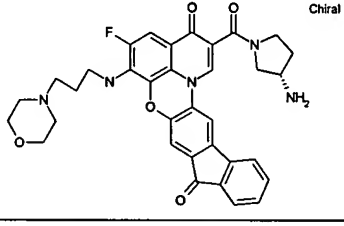
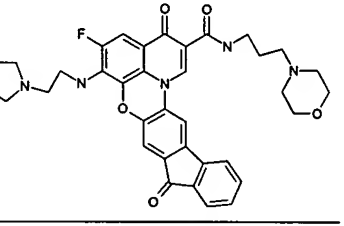
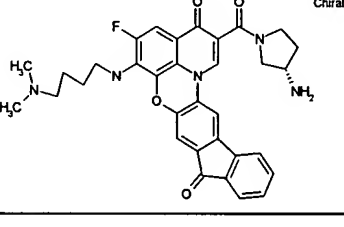
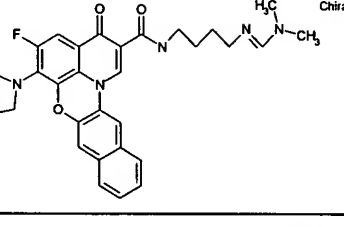
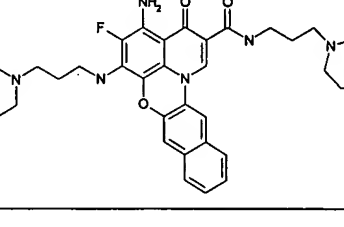
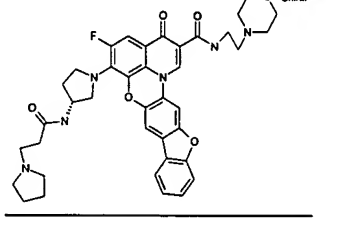
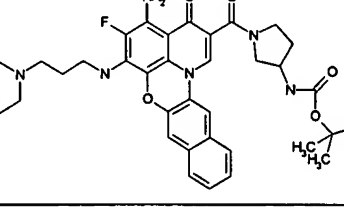
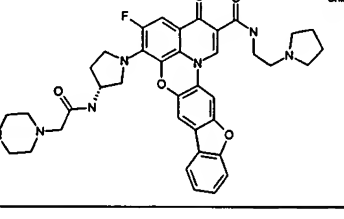
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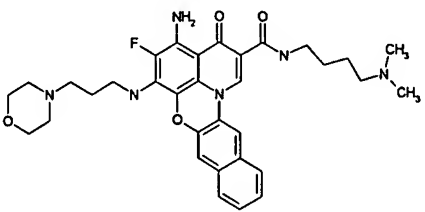
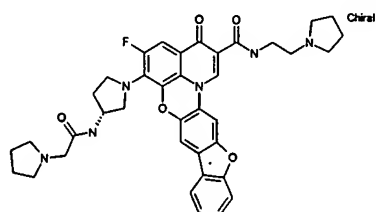
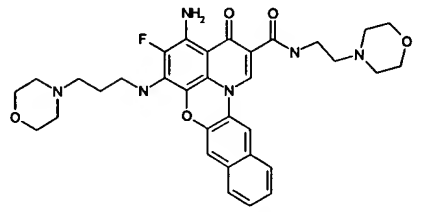
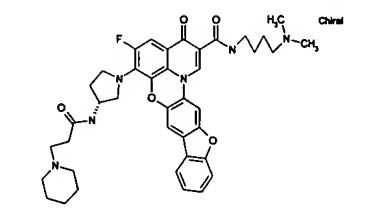
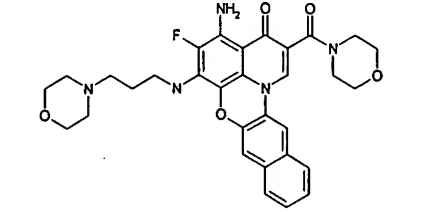
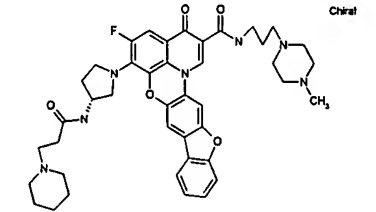
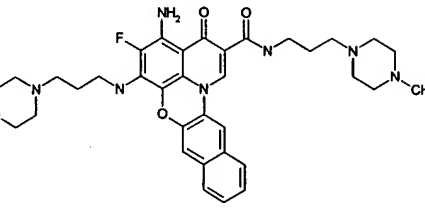
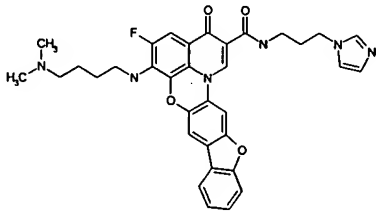
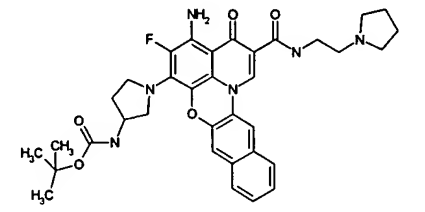
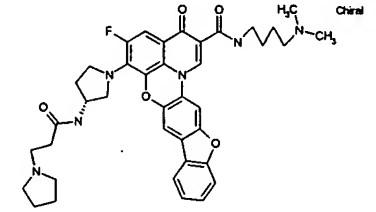
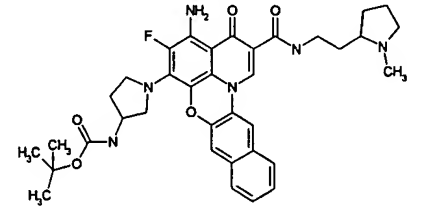
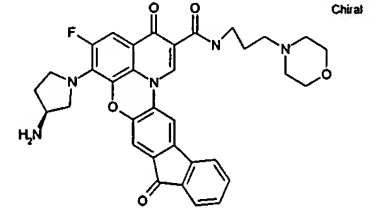
	
	
	
	
	
	

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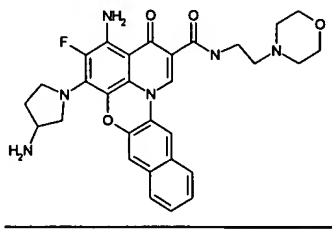
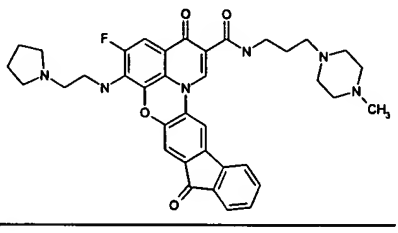
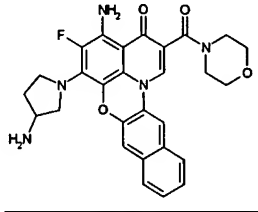
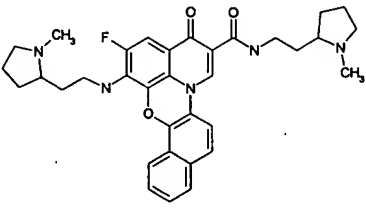
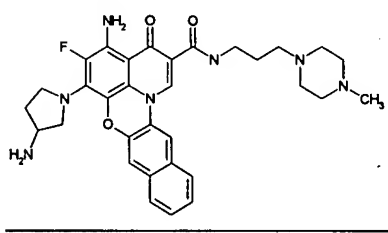
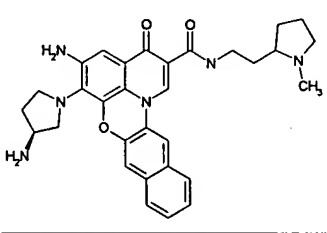
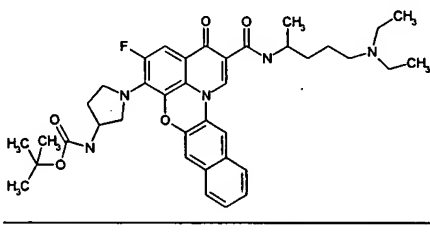
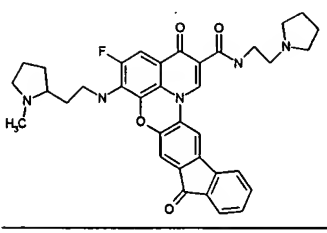
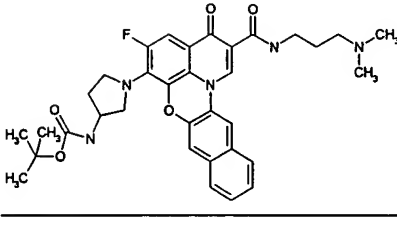
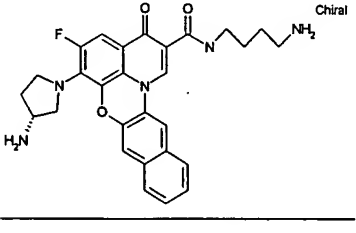
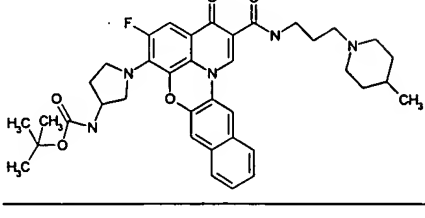
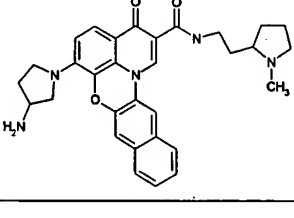
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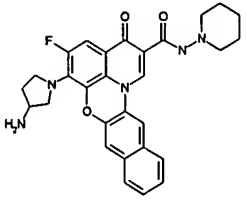
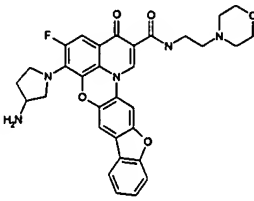
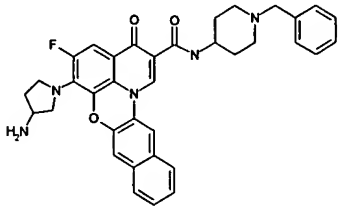
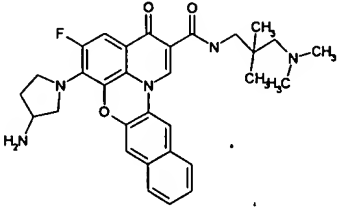
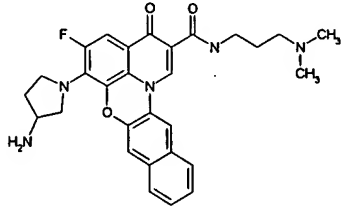
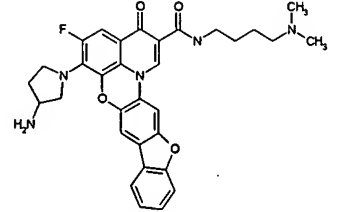
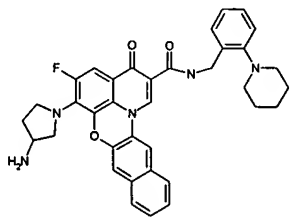
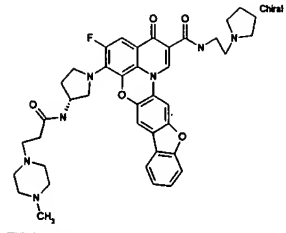
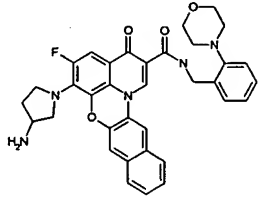
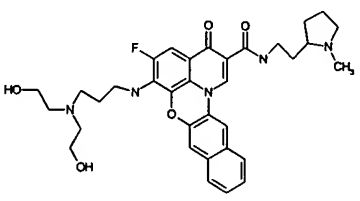
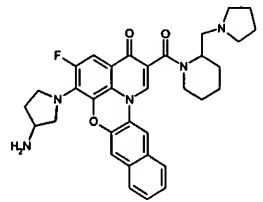
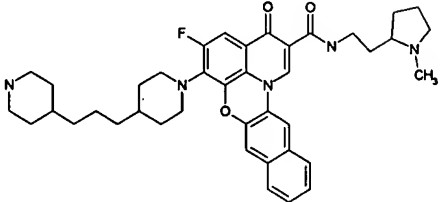


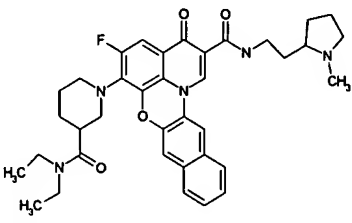
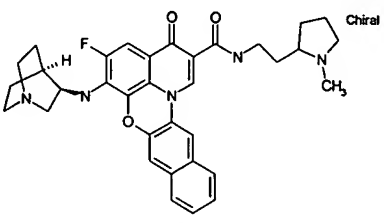
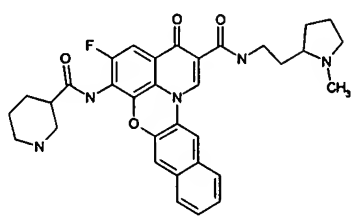
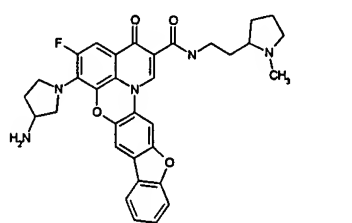
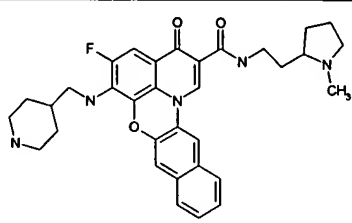
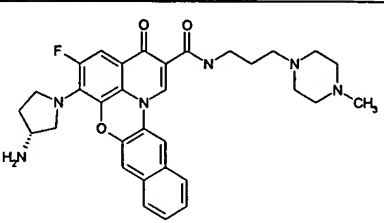
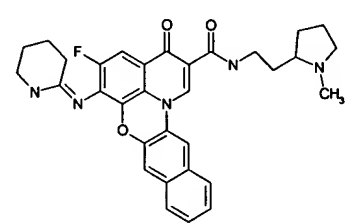
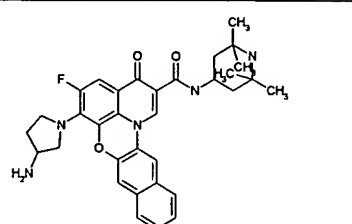
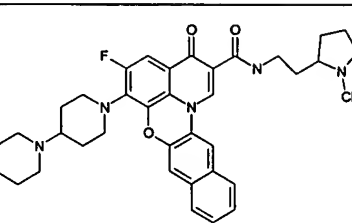
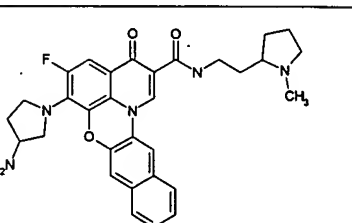
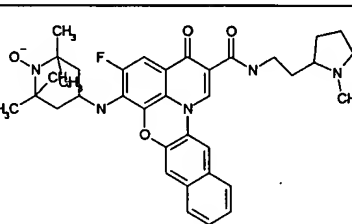
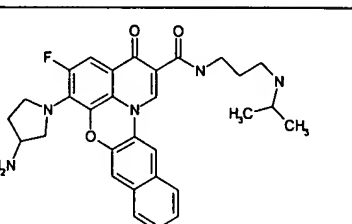
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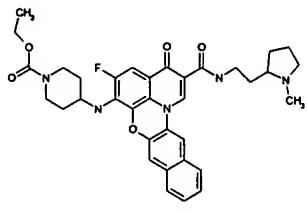
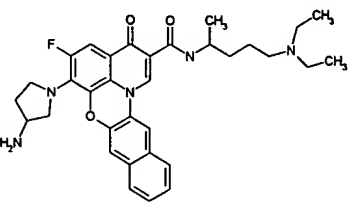
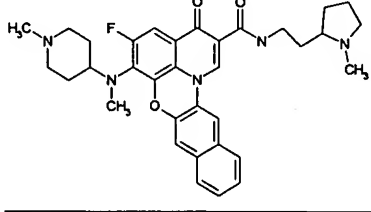
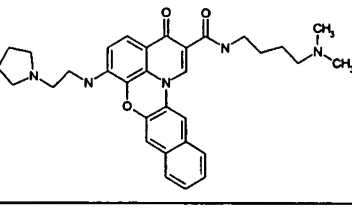
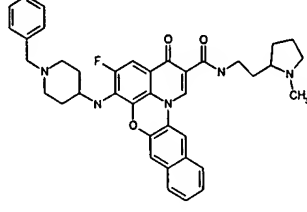
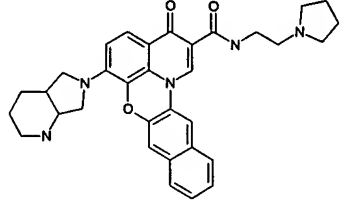
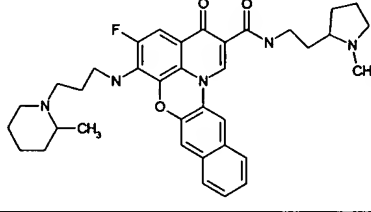
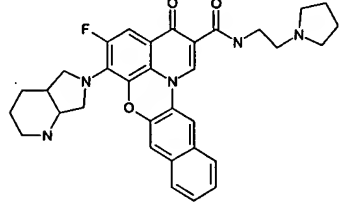
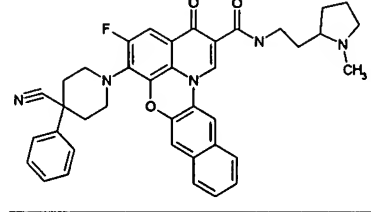
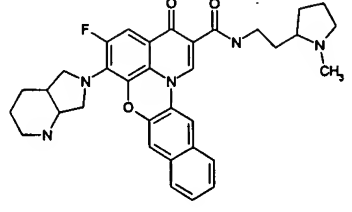
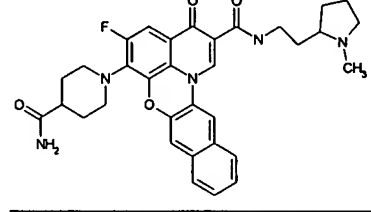
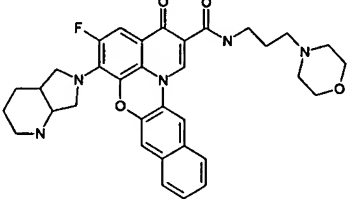
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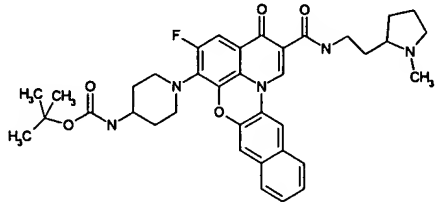
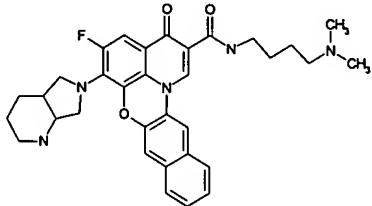
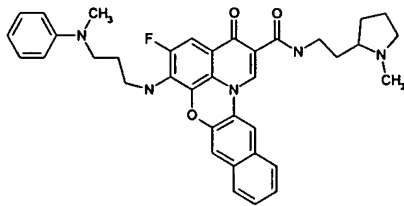
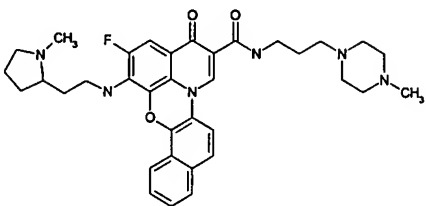
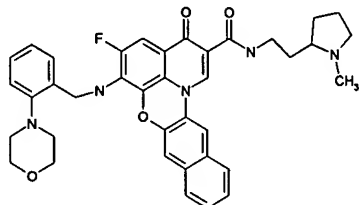
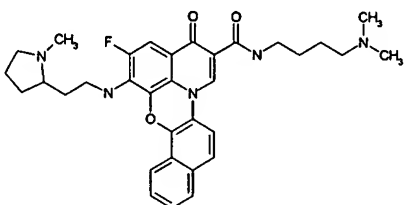
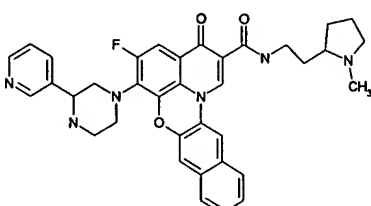
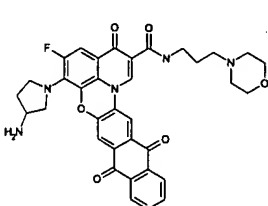
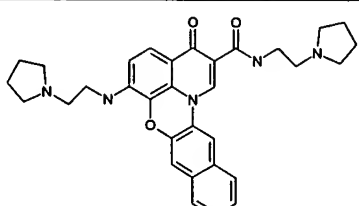
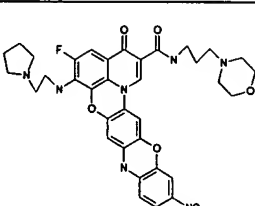
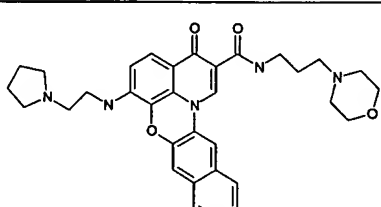
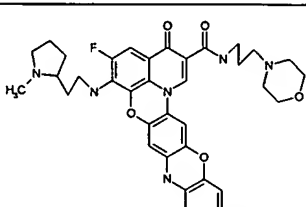
	
	
	
	
	
	

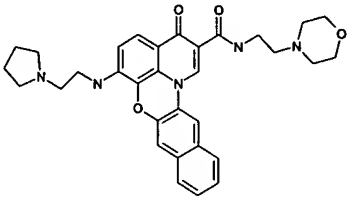
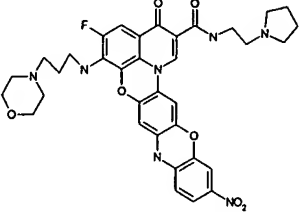
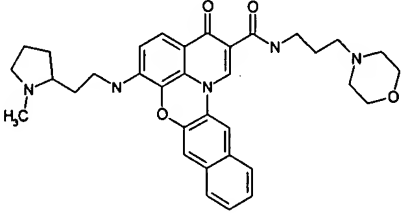
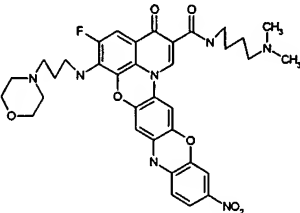
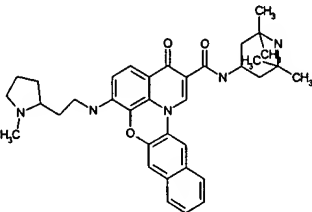
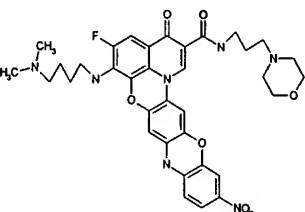
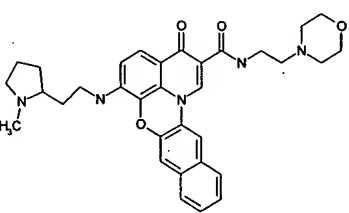
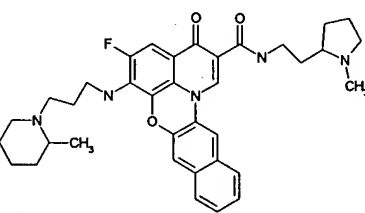
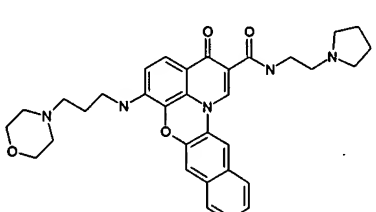
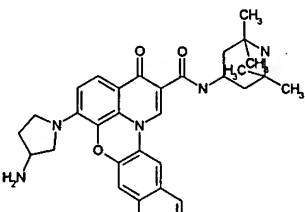
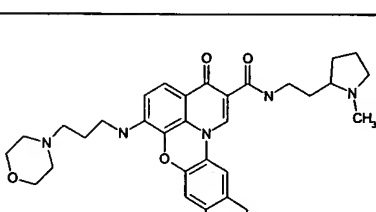
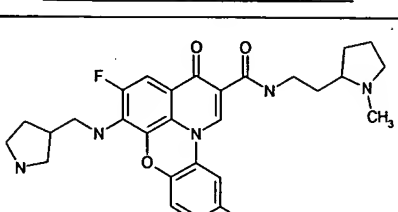
	
	
	
	
	
	

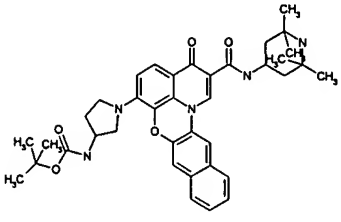
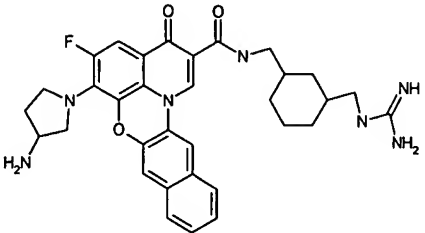
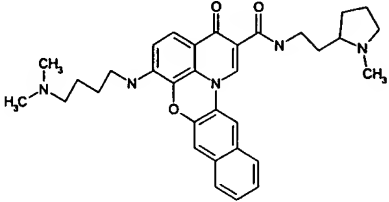
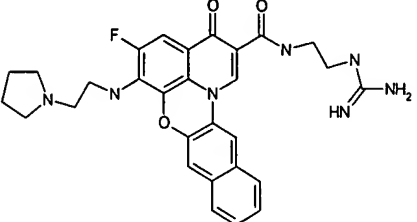
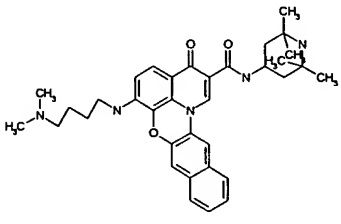
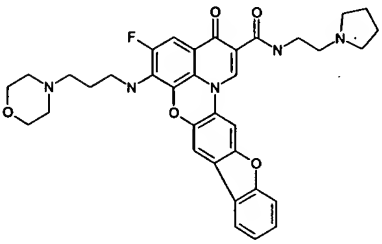
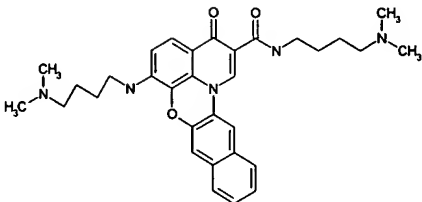
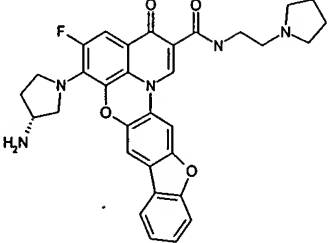
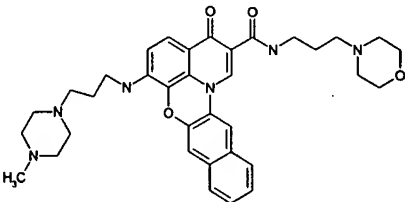
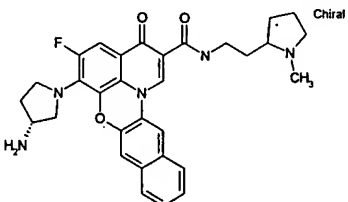
	
	
	
	
	
	

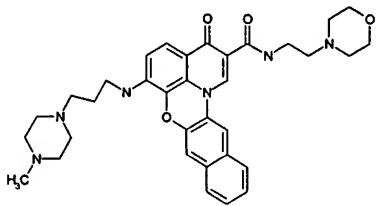
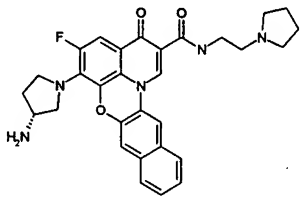
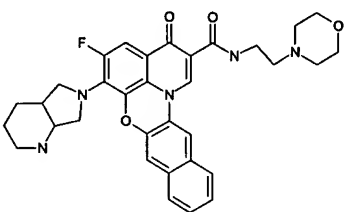
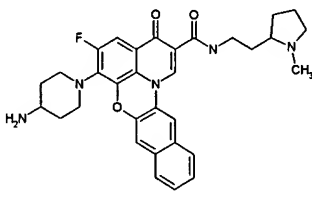
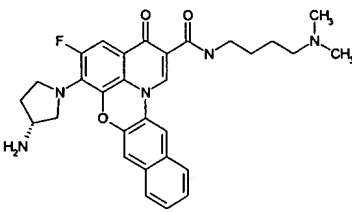
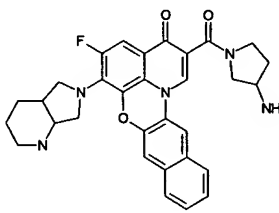
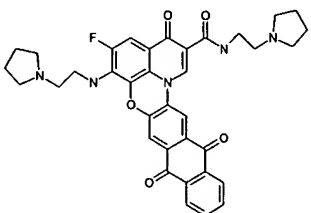
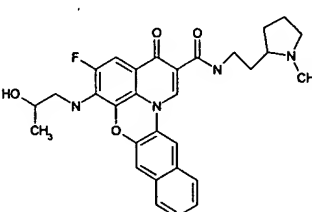
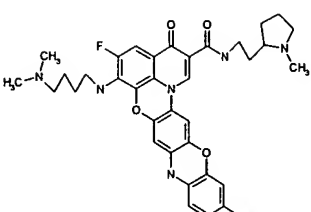
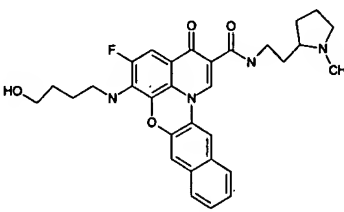
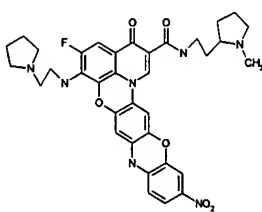
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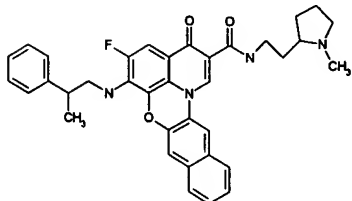
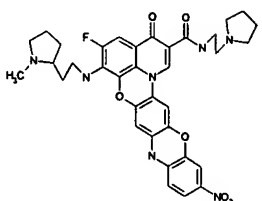
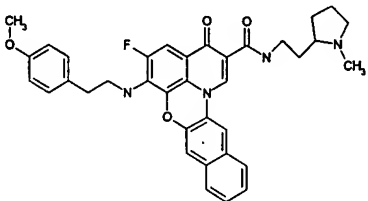
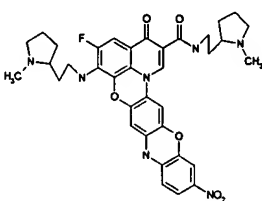
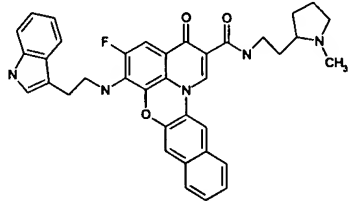
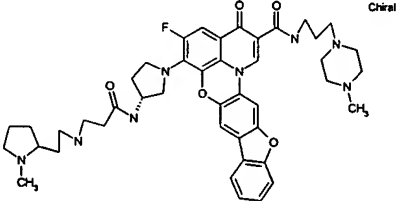
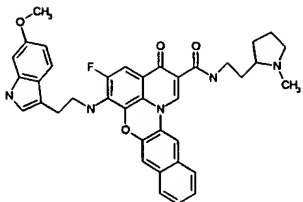
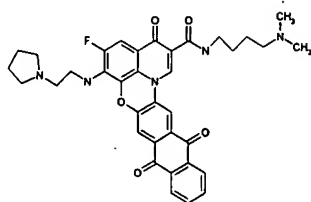
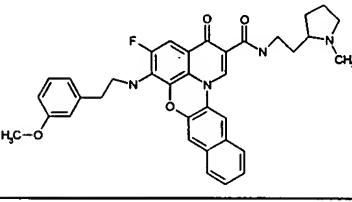
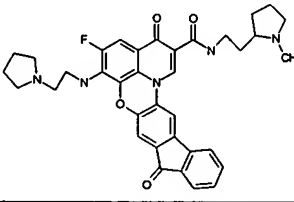
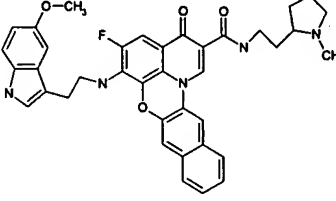
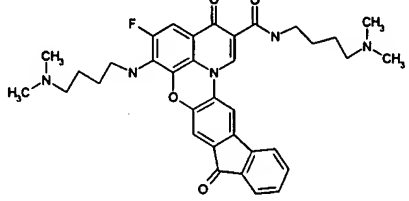


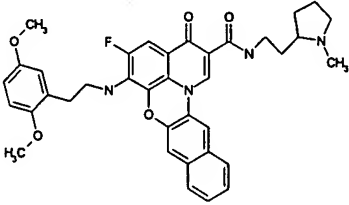
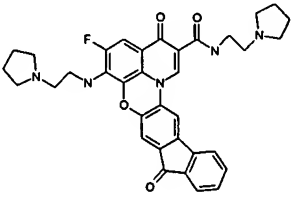
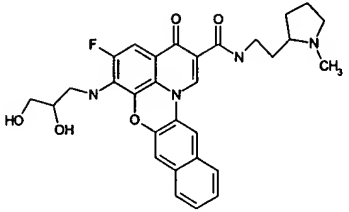
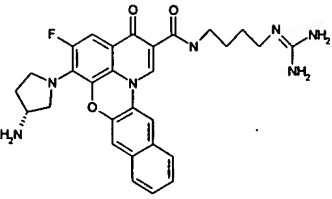
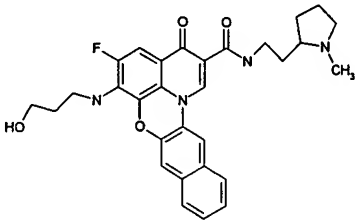
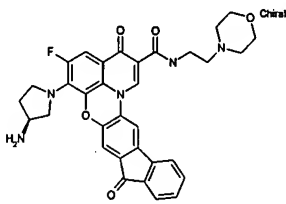
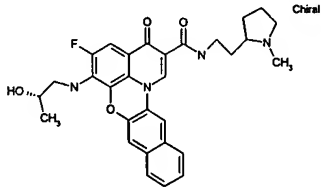
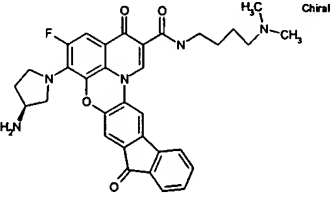
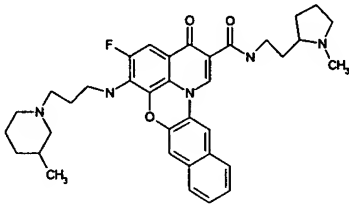
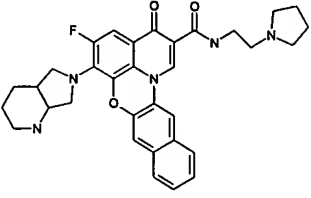
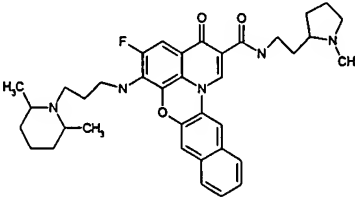
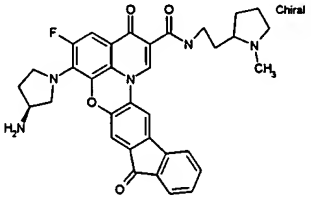
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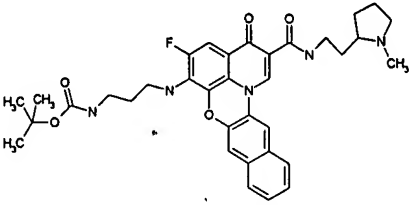
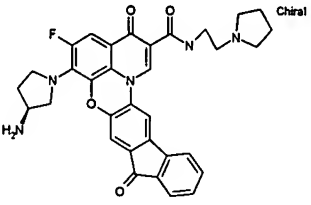
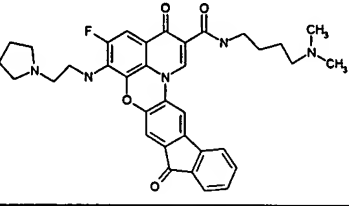
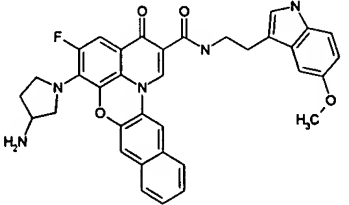
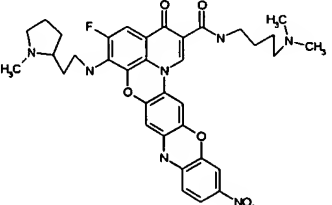
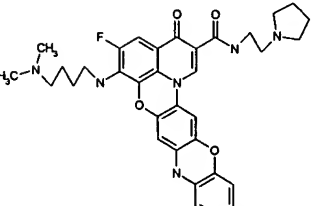
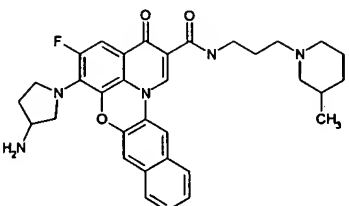
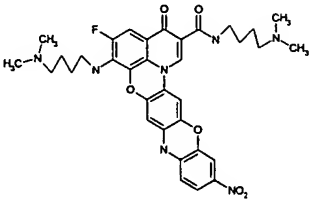
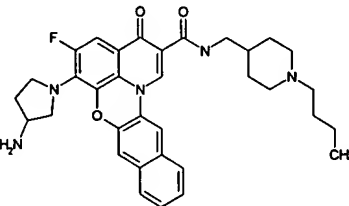
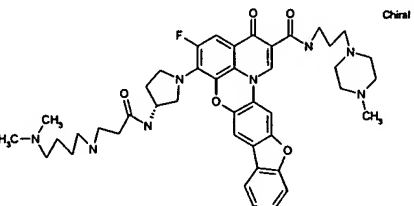
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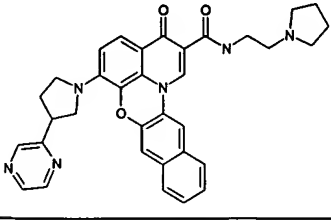
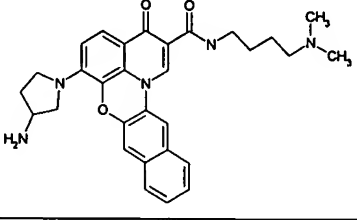
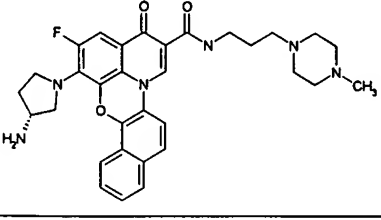
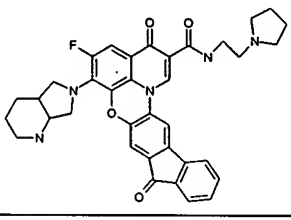
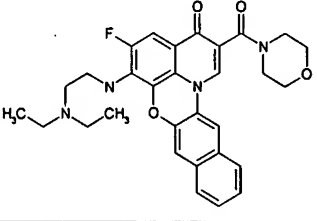
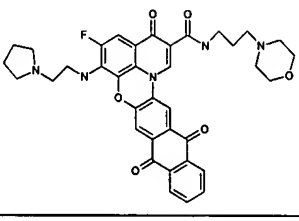
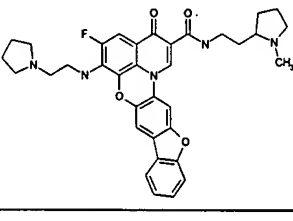
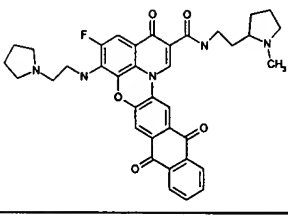
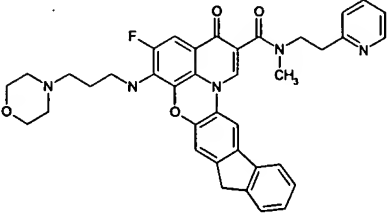
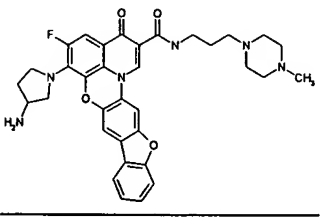
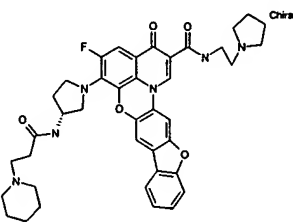
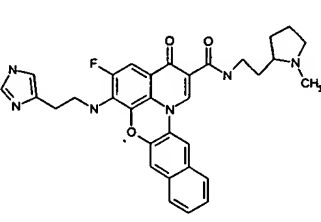
	
	
	
	
	

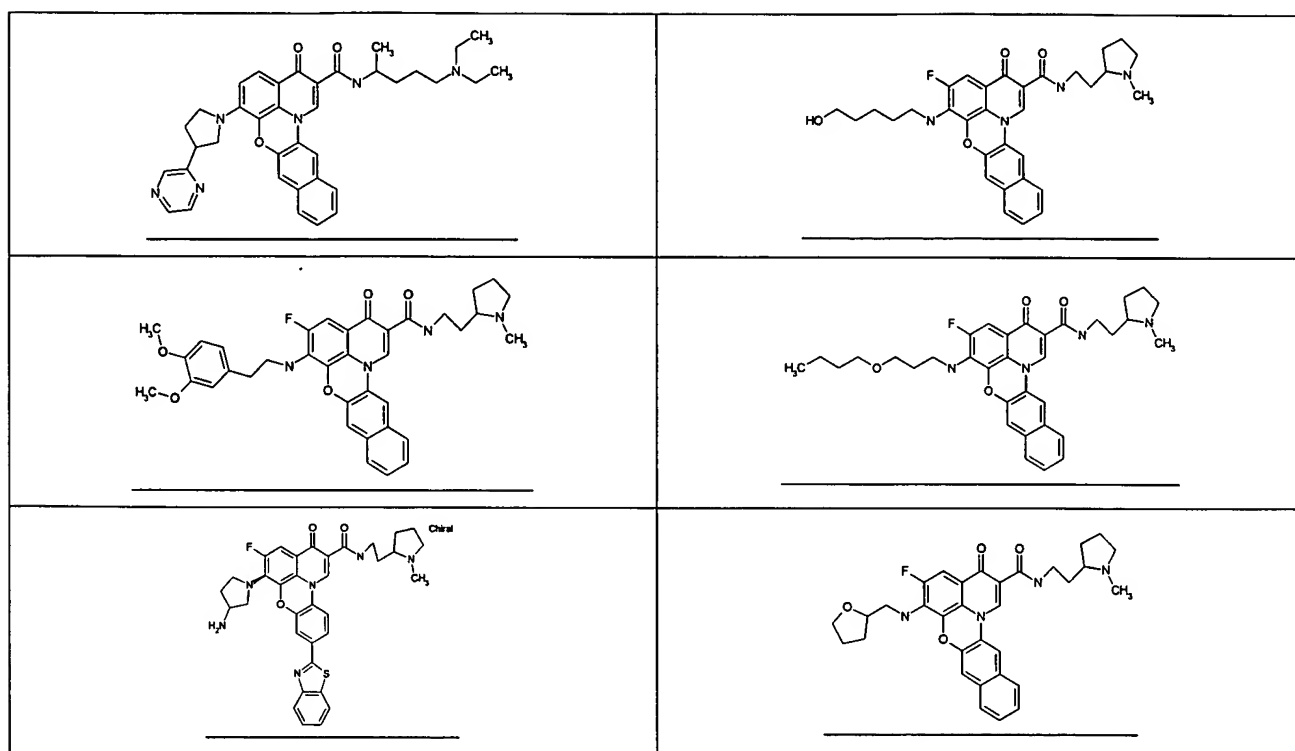
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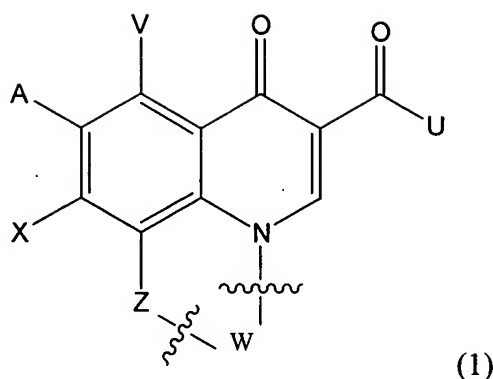




47. (new). The compound of claim 1, wherein R is a C<sub>1-10</sub> alkyl substituted with a 5-14 membered heterocyclic ring.

48. (new). The compound of claim 47, wherein the heterocyclic ring is selected from the group consisting of pyrrolidine, imidazole, pyridine, morpholine, thiomorpholine, piperazine, piperidine and diazepine.

49. (new). A compound having formula 1,



and pharmaceutically acceptable salts, esters and prodrugs thereof;

wherein V is H, halo, or  $\text{NR}^1\text{R}^2$ ;

A is H, fluoro, or  $\text{NR}^1_2$ ;

Z is O;

U is OR or  $\text{NR}^1\text{R}^2$ ;

X is  $\text{OR}^2$ ,  $\text{NR}^1\text{R}^2$ , halo, azido, or  $\text{SR}^2$ ;

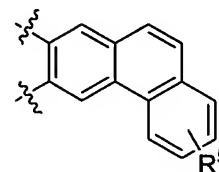
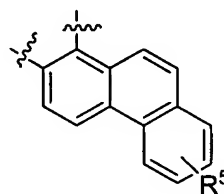
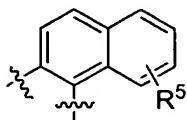
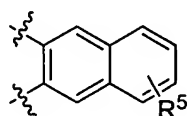
wherein  $\text{R}^1$  and  $\text{R}^2$  together with N in  $\text{NR}^1\text{R}^2$  may form an optionally substituted 5-6 membered ring optionally containing one or more heteroatoms selected from N, O and S;

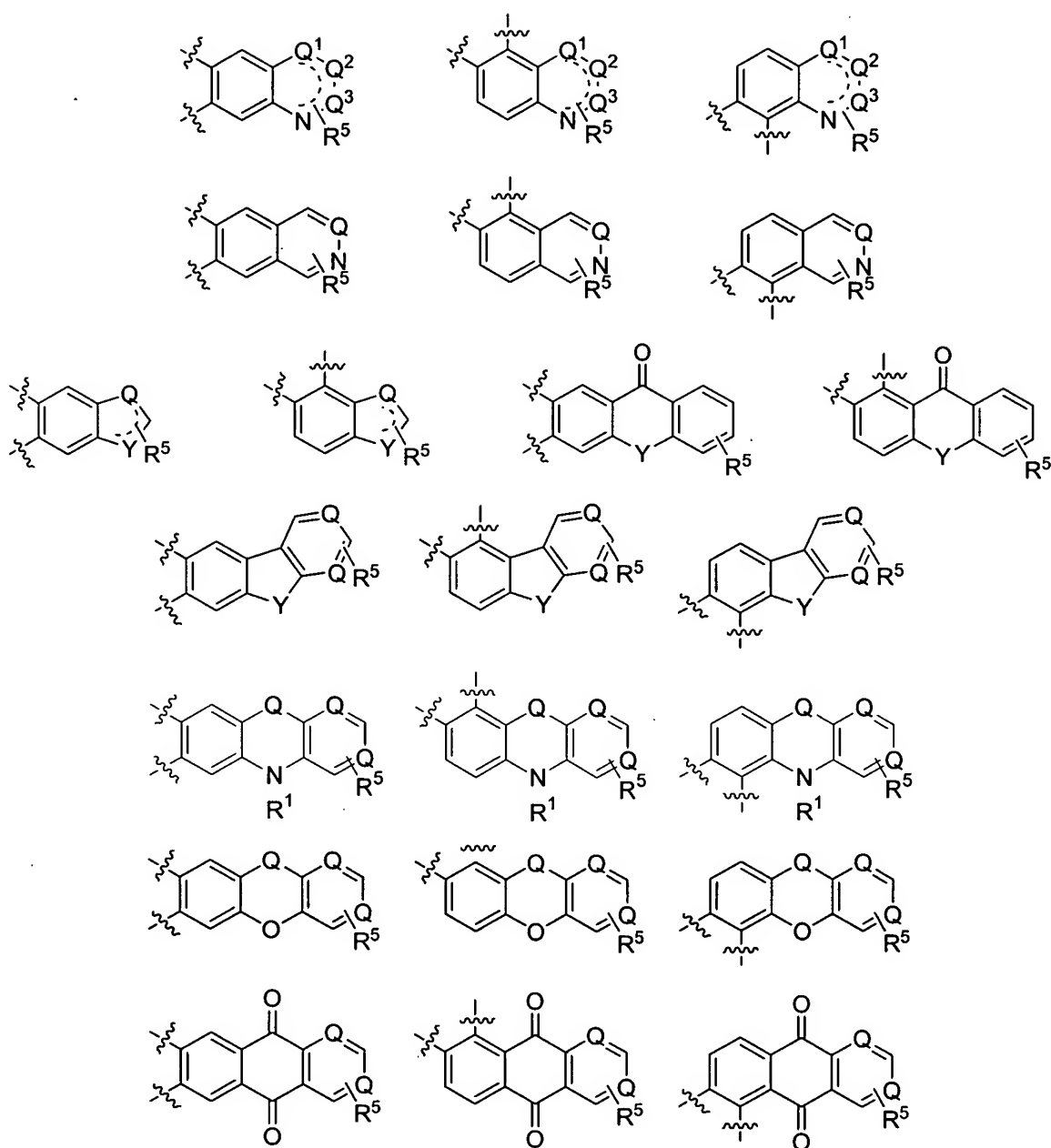
R is an optionally substituted heterocyclic ring, aryl or heteroaryl; a  $\text{C}_{1-10}$  alkyl substituted with a carbocyclic or heterocyclic ring, and optionally containing one or more non-adjacent heteroatoms selected from N, O, and S; or an optionally substituted  $\text{C}_{2-10}$  alkenyl;

$\text{R}^1$  is H or a  $\text{C}_{1-6}$  alkyl;

$\text{R}^2$  is H or a  $\text{C}_{1-10}$  alkyl or  $\text{C}_{2-10}$  alkenyl optionally containing one or more non-adjacent heteroatoms selected from N, O, and S, and optionally substituted with a carbocyclic or heterocyclic ring; or  $\text{R}^2$  is an optionally substituted heterocyclic ring, aryl or heteroaryl;

W is selected from the group consisting of





wherein Q, Q<sup>1</sup>, Q<sup>2</sup>, and Q<sup>3</sup> are independently CH or N;

Y is independently O, CH, C=O or NR<sup>1</sup>;

and R<sup>5</sup> is a substituent at any position on the fused ring; and is H, OR<sup>2</sup>, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, each optionally substituted by halo, or C=O; or two adjacent R<sup>5</sup> is linked to obtain a 5-6 membered substituted or unsubstituted carbocyclic or heterocyclic ring, optionally fused to an additional substituted or unsubstituted carbocyclic or heterocyclic ring;

wherein each optionally substituted moiety is substituted with one or more halo, OR<sup>2</sup>, NR<sup>1</sup>R<sup>2</sup>, carbamate, C<sub>1-10</sub> alkyl, C<sub>2-10</sub> alkenyl, each optionally substituted by halo, C=O, aryl or one or more heteroatoms selected from N, O and S; or is substituted with an aryl, a carbocyclic or a heterocyclic ring.

50. (new) The compound of claim 49, wherein A and X are independently halo.
51. (new) The compound of claim 49, wherein said halo is fluoro.
52. (new) The compound of claim 49, where V is H.
53. (new) The compound of claim 49, wherein U and X are independently NR<sup>1</sup>R<sup>2</sup>.
54. (new) The compound of claim 53, wherein R<sup>1</sup> is H and R<sup>2</sup> is a C<sub>1-10</sub> alkyl optionally containing N, O or S, and optionally substituted with a C<sub>3-6</sub> cycloalkyl, aryl or a 5-14 membered heterocyclic ring containing one or more N, O or S.
55. (new) The compound of claim 54, wherein said 5-14 membered heterocyclic ring is selected from the group consisting of tetrahydrofuran, 1,3-dioxolane, 2,3-dihydrofuran, tetrahydropyran, benzofuran, isobenzofuran, 1,3-dihydro-isobenzofuran, isoxazole, 4,5-dihydroisoxazole, piperidine, pyrrolidine, pyrrolidin-2-one, pyrrole, pyridine, pyrimidine, octahydro-pyrrolo[3,4-*b*]pyridine, piperazine, pyrazine, morpholine, thiomorpholine, imidazole, imidazolidine-2,4-dione, benzimidazole, 1,3-dihydrobenzimidazol-2-one, indole, thiazole, benzothiazole, thiadiazole, thiophene, tetrahydro-thiophene 1,1-dioxide, diazepine, triazole, guanidine, diazabicyclo[2.2.1]heptane, 2,5-diazabicyclo[2.2.1]heptane, and 2,3,4,4a,9,9a-hexahydro-1H- $\beta$ -carboline.
56. (new) The compound of claim 54, wherein R<sup>1</sup> is H and R<sup>2</sup> is an aryl or a 5-14 membered heterocyclic ring containing one or more N, O or S, each optionally substituted with an amino or another heterocyclic ring.

57. (new) The compound of claim 56, wherein said 5-14 membered heterocyclic ring is selected from the group consisting of tetrahydrofuran, 1,3-dioxolane, 2,3-dihydrofuran, tetrahydropyran, benzofuran, isobenzofuran, 1,3-dihydro-isobenzofuran, isoxazole, 4,5-dihydroisoxazole, piperidine, pyrrolidine, pyrrolidin-2-one, pyrrole, pyridine, pyrimidine, octahydro-pyrrolo[3,4-b]pyridine, piperazine, pyrazine, morpholine, thiomorpholine, imidazole, imidazolidine-2,4-dione, benzimidazole, 1,3-dihydrobenzimidazol-2-one, indole, thiazole, benzothiazole, thiadiazole, thiophene, tetrahydro-thiophene 1,1-dioxide, diazepine, triazole, guanidine, diazabicyclo[2.2.1]heptane, 2,5-diazabicyclo[2.2.1]heptane, and 2,3,4,4a,9a-hexahydro-1H- $\beta$ -carboline.

58. (new) The compound of claim 53, wherein  $R^1$  and  $R^2$  together with N in  $NR^1R^2$  form an optionally substituted 5-6 membered ring containing one or more N, O or S.

59. (new) The compound of claim 58, where  $NR^1R^2$  is pyrrolidine, imidazole, pyridine, morpholine, thiomorpholine, piperazine, piperidine or diazepine.

60. (new) The compound of claim 49, wherein X is  $NR^1R^2$ , and  $R^1$  and  $R^2$  together with N form a substituted 5-6 membered ring containing one or more N, O or S.

61. (new) The compound of claim 60, wherein X is optionally substituted with amino, carbamate, a  $C_{1-10}$  alkyl containing one or more non-adjacent N, O or S, and optionally substituted with a heterocyclic ring; aryl or a saturated or unsaturated heterocyclic ring, each of which is optionally substituted.

62. (new) The compound of claim 61, wherein X is substituted with a heterocyclic ring selected from the group consisting of tetrahydrofuran, 1,3-dioxolane, 2,3-dihydrofuran, tetrahydropyran, benzofuran, isobenzofuran, 1,3-dihydro-isobenzofuran, isoxazole, 4,5-dihydroisoxazole, piperidine, pyrrolidine, pyrrolidin-2-one, pyrrole, pyridine, pyrimidine, octahydro-pyrrolo[3,4-b]pyridine, piperazine, pyrazine, morpholine, thiomorpholine, imidazole, imidazolidine-2,4-dione, benzimidazole, 1,3-dihydrobenzimidazol-2-one, indole, thiazole,

benzothiazole, thiadiazole, thiophene, tetrahydro-thiophene 1,1-dioxide, diazepine, triazole, guanidine, diazabicyclo[2.2.1]heptane, 2,5-diazabicyclo[2.2.1]heptane, and 2,3,4,4a,9,9a-hexahydro-1H- $\beta$ -carboline.

63. (new) The compound of claim 60, wherein X is morpholine, thiomorpholine, imidazole, pyrrolidine, piperazine, pyridine or piperidine.

64. (new) The compound of claim 63, wherein X is pyrrolidine.

65. (new) A pharmaceutical composition comprising the compound of claim 49 and a pharmaceutically acceptable excipient.